

Overview of PM_{2.5}-Related Mortality Studies

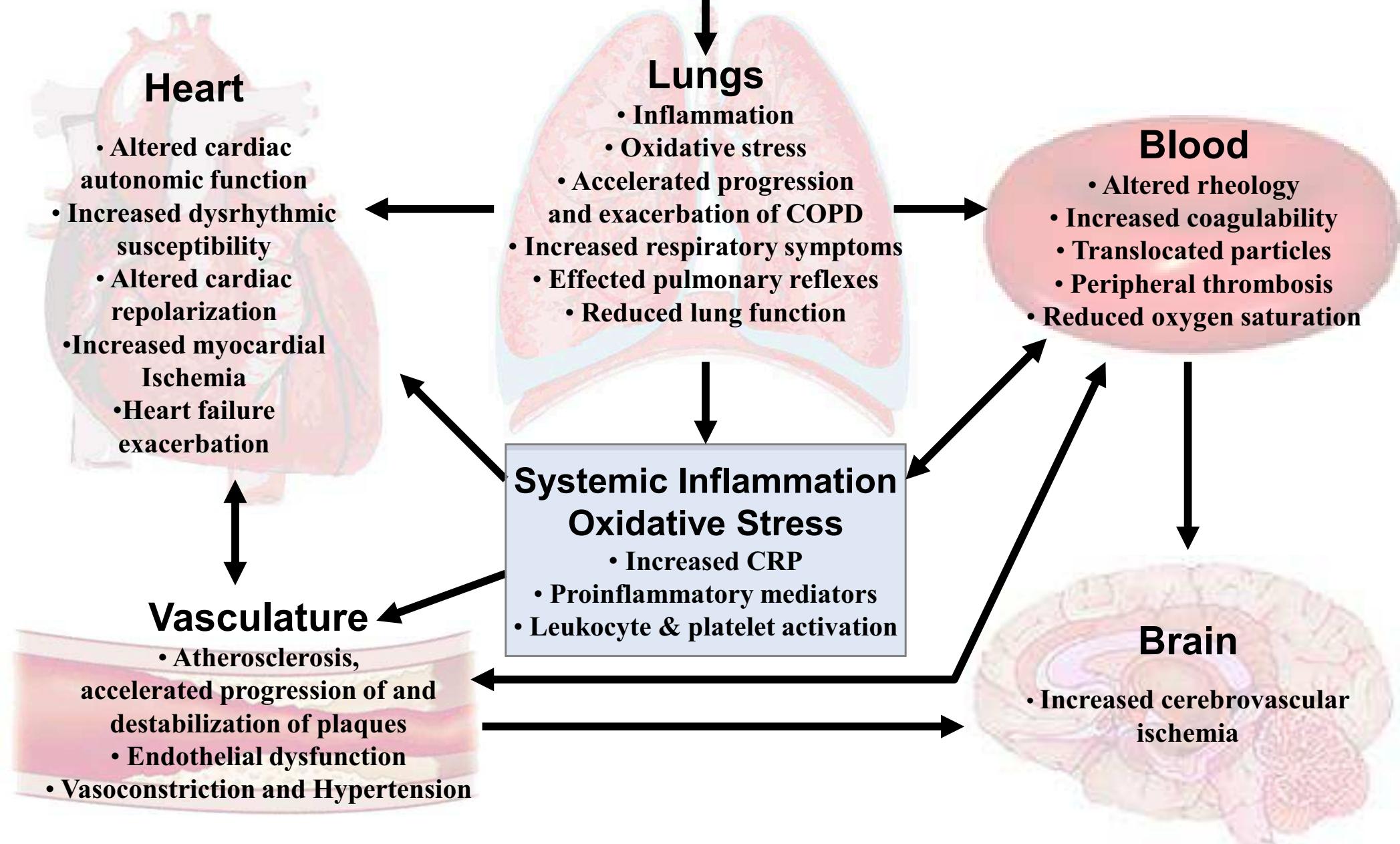
C. Arden Pope III, PhD

Mary Lou Fulton Professor
Brigham Young University

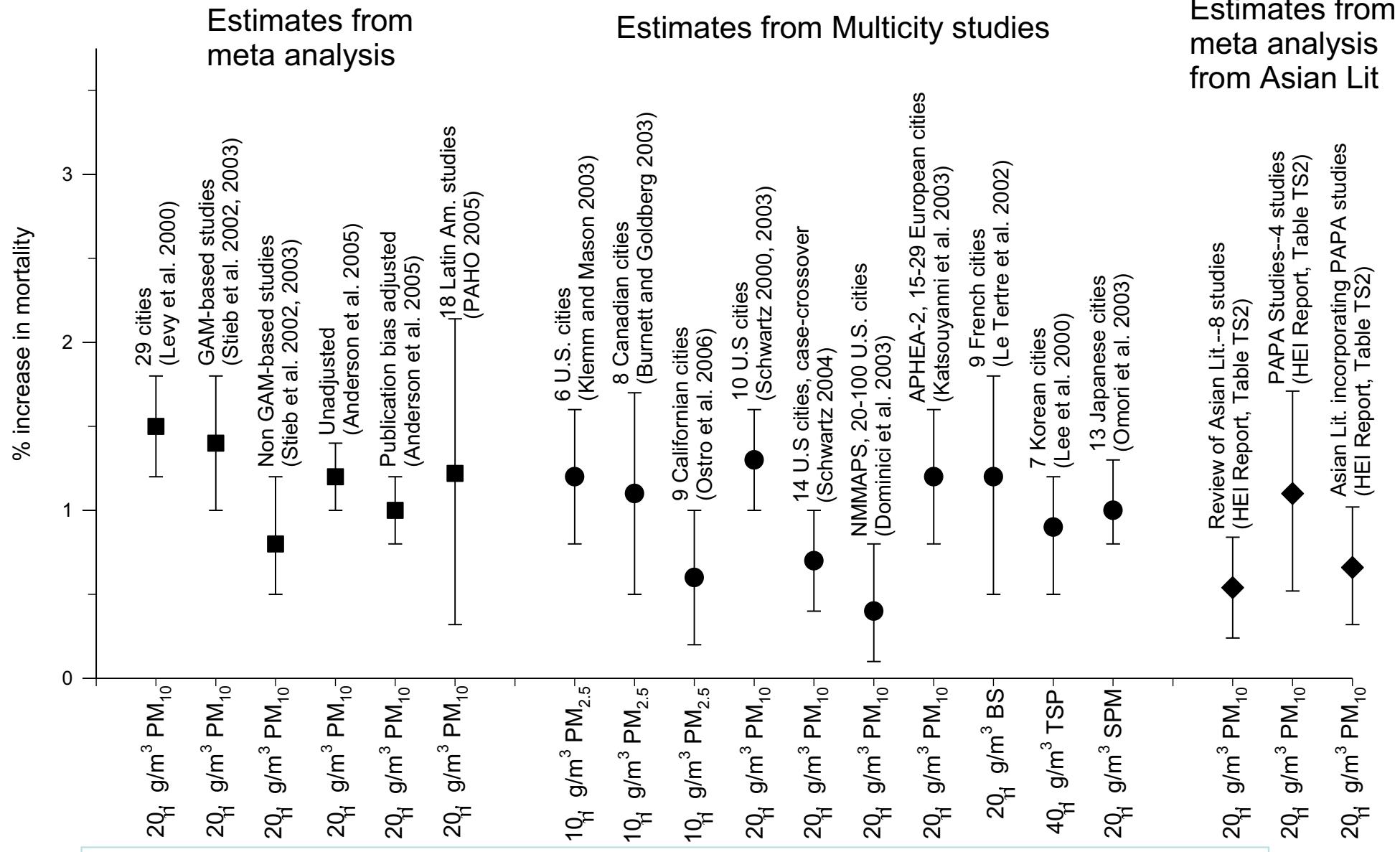
Presented at: ARB Symposium

Methodology for Estimating Premature Deaths from PM2.5 Exposure
Sacramento, CA
February 26, 2010

PM Inhalation



Daily time-series studies ***of over 200 cities***



10 $\mu\text{g}/\text{m}^3 \text{ PM}_{2.5}$ or 20 $\mu\text{g}/\text{m}^3 \text{ PM}_{10} \rightarrow 0.4\% \text{ to } 1.5\%$
increase in relative risk of mortality—Small but
 remarkably consistent across meta-analyses and multi-city studies.

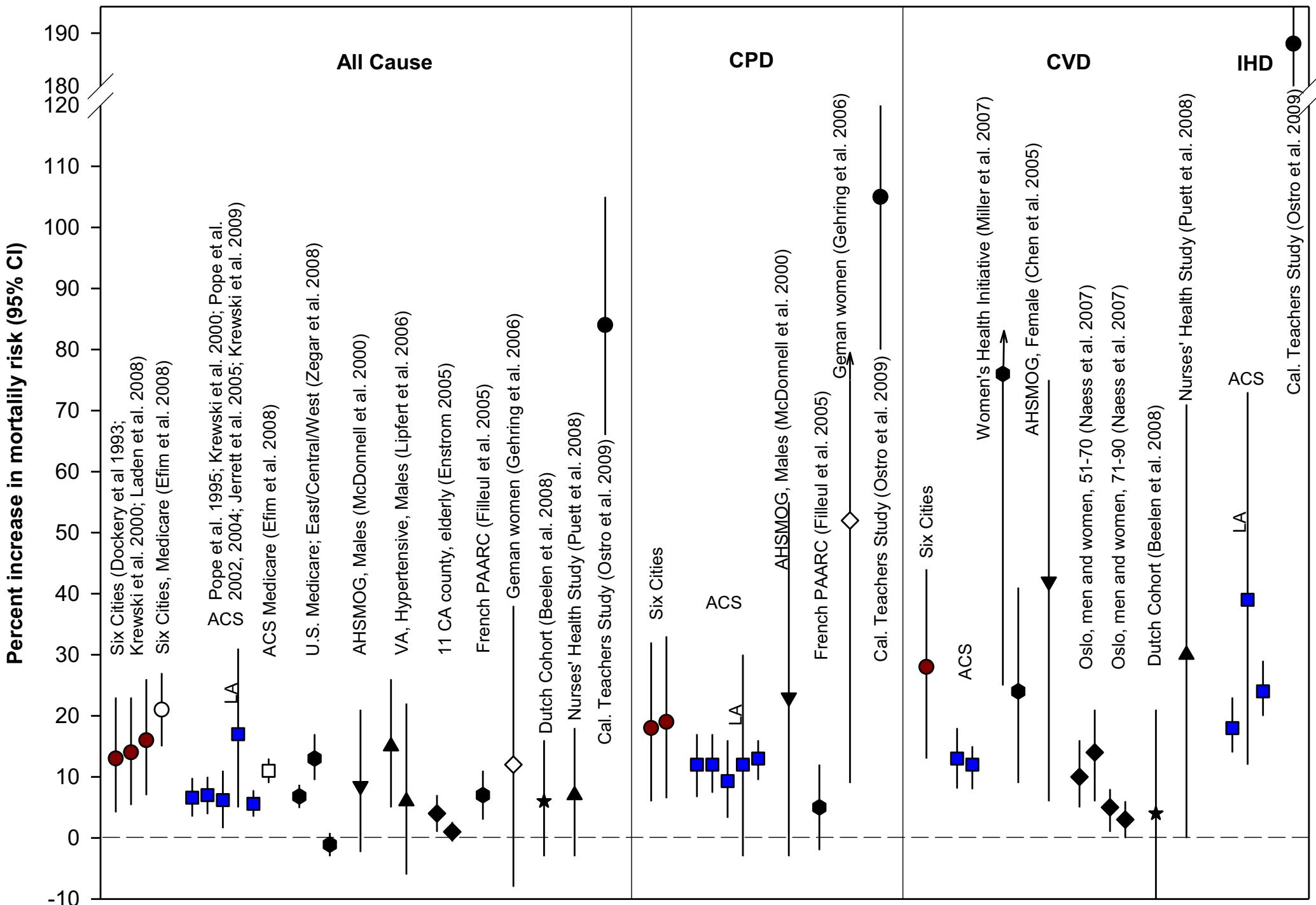
Overall literature is now far too massive to review in a short presentation.

The objective of this presentation:

Focus on the most relevant studies to estimate overall mortality effects

--cohort studies of long-term exposure.

Summary of published cohort and related studies of long-term fine PM exposure. Percent increases in mortality and related risk (95% CIs) associated with $10 \mu\text{g}/\text{m}^3 \text{PM}_{2.5}$ (or other as indicated).



An Association Between Air Pollution and Mortality in Six U.S. Cities



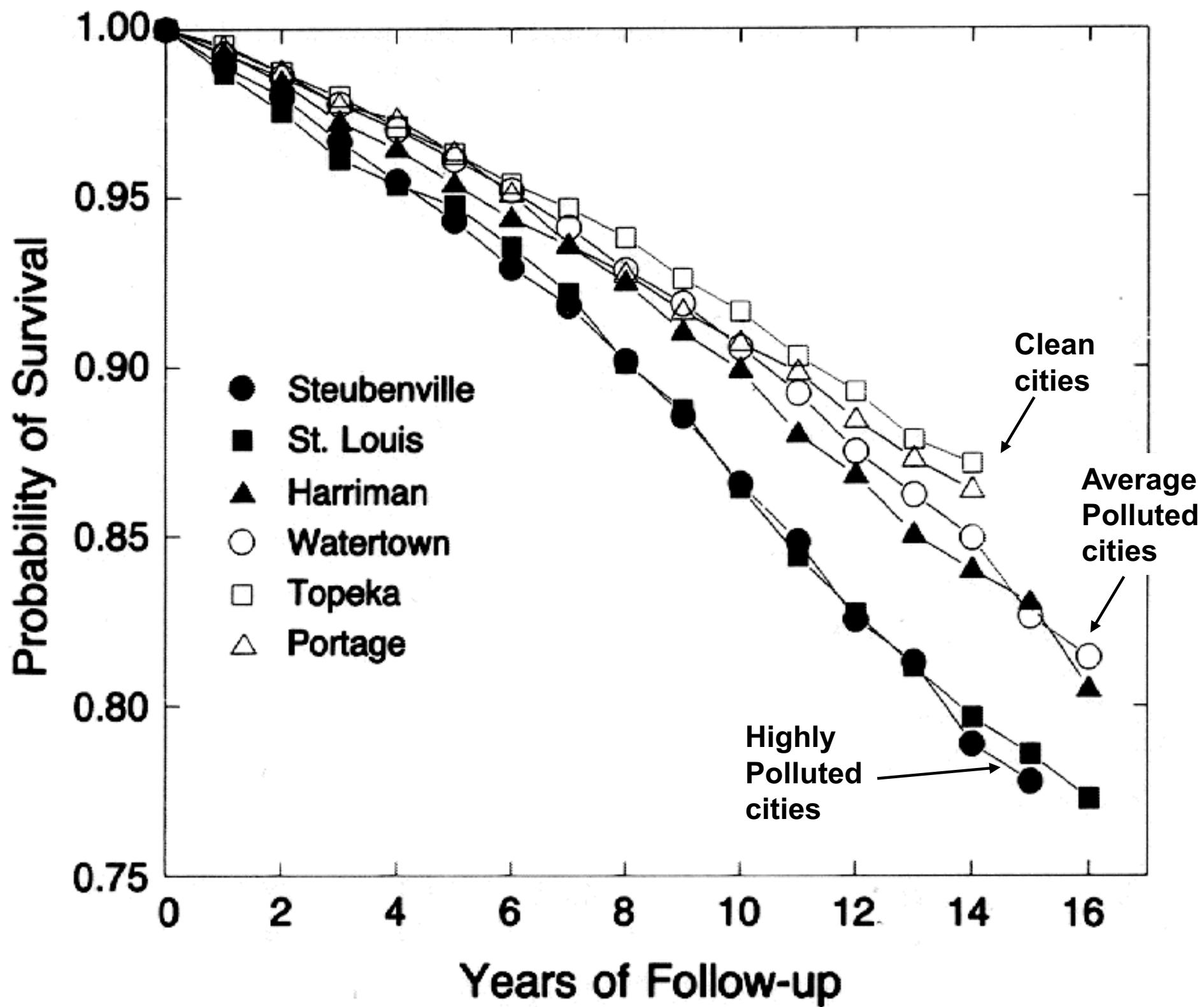
The NEW ENGLAND
JOURNAL of MEDICINE 1993

Dockery DW, Pope CA III, Xu X, Spengler JD,
Ware JH, Fay ME, Ferris BG Jr, Speizer FE.



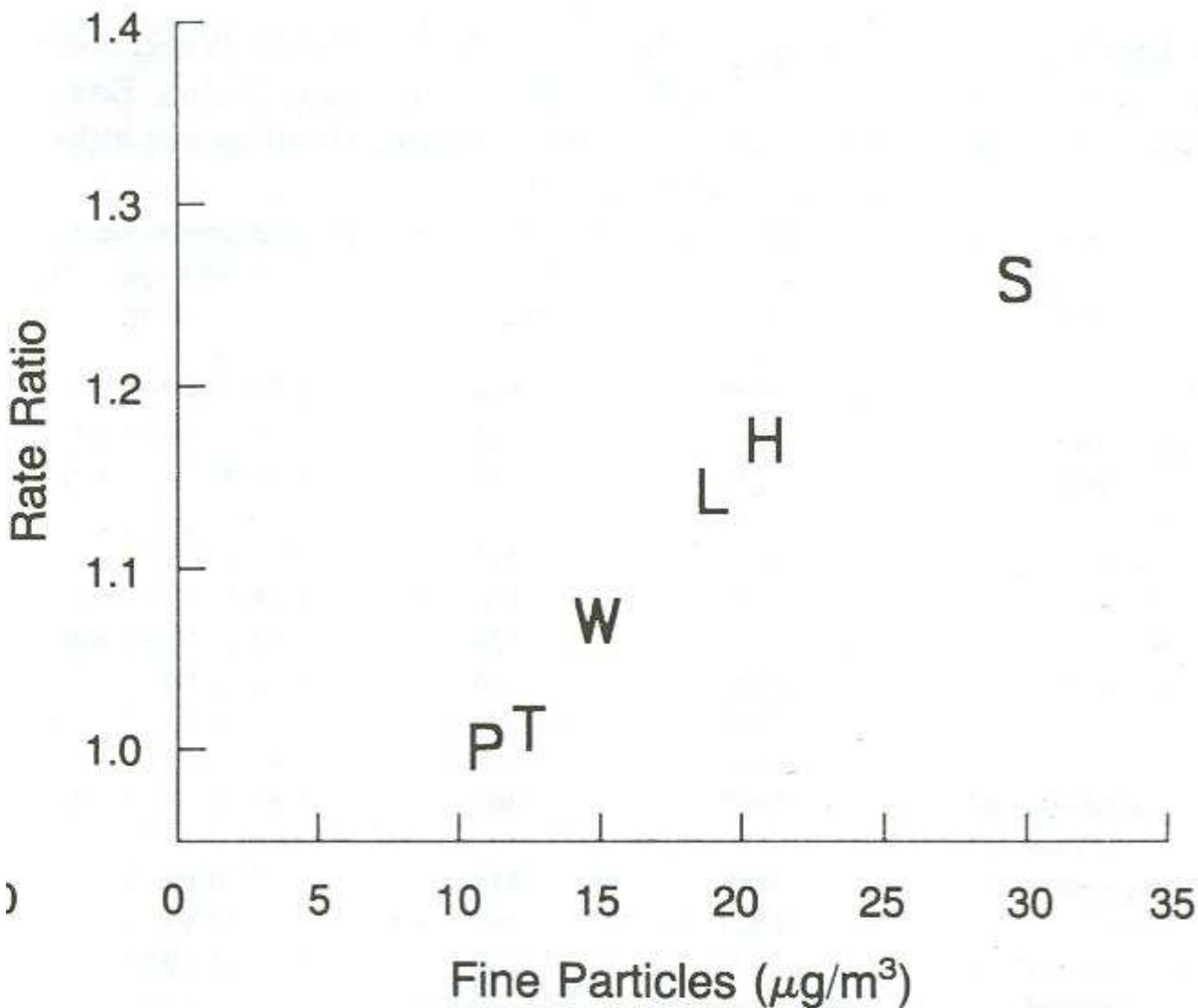
Methods:

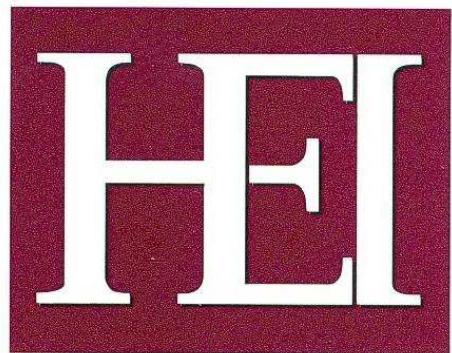
- 14-16 yr prospective follow-up of 8,111 adults living in six U.S. cities.
- Monitoring of TSP PM₁₀, PM_{2.5}, SO₄, H⁺, SO₂, NO₂, O₃.
- Data analyzed using survival analysis, including Cox Proportional Hazards Models.
- Controlled for individual differences in: age, sex, smoking, BMI, education, occupational exposure.



Adjusted risk ratios (and 95% CIs) for cigarette smoking and PM_{2.5}

Cause of Death	Current Smoker, 25 Pack years	Most vs. Least Polluted City
All	2.00 (1.51-2.65)	1.26 (1.08-1.47)
Lung Cancer	8.00 (2.97-21.6)	1.37 (0.81-2.31)
Cardio-pulmonary	2.30 (1.56-3.41)	1.37 (1.11-1.68)
All other	1.46 (0.89-2.39)	1.01 (0.79-1.30)





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July 2000



Dan Krewski
Rick Burnett
Mark Goldberg
and 28 others

SPECIAL REPORT

Reanalysis of the Harvard Six Cities Study and the American Cancer Society Study of Particulate Air Pollution and Mortality

A Special Report of the Institute's Particle Epidemiology Reanalysis Project

Six-Cities:
Extended analyses:
Laden et al. AJRCCM 2006

Effect of dose and timing:
Schwartz, et al EHP 2008

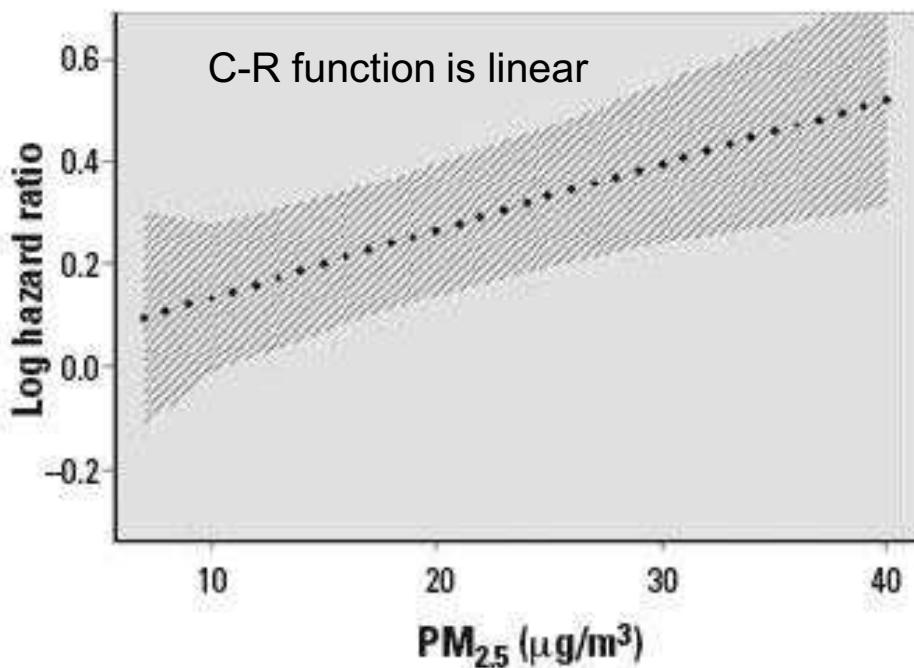


Figure 2. The estimated concentration-response relation between PM_{2.5} and the risk of death in the Six Cities Study, based on averaging the 32 possible models that were fit. Also shown are the pointwise 95% CIs around that curve, based on jackknife estimates.

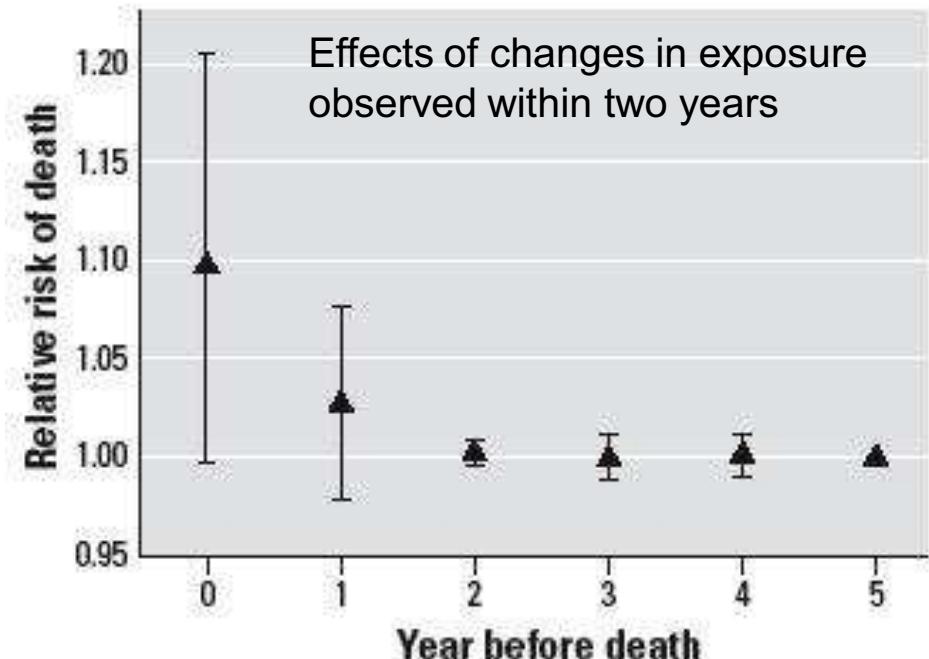
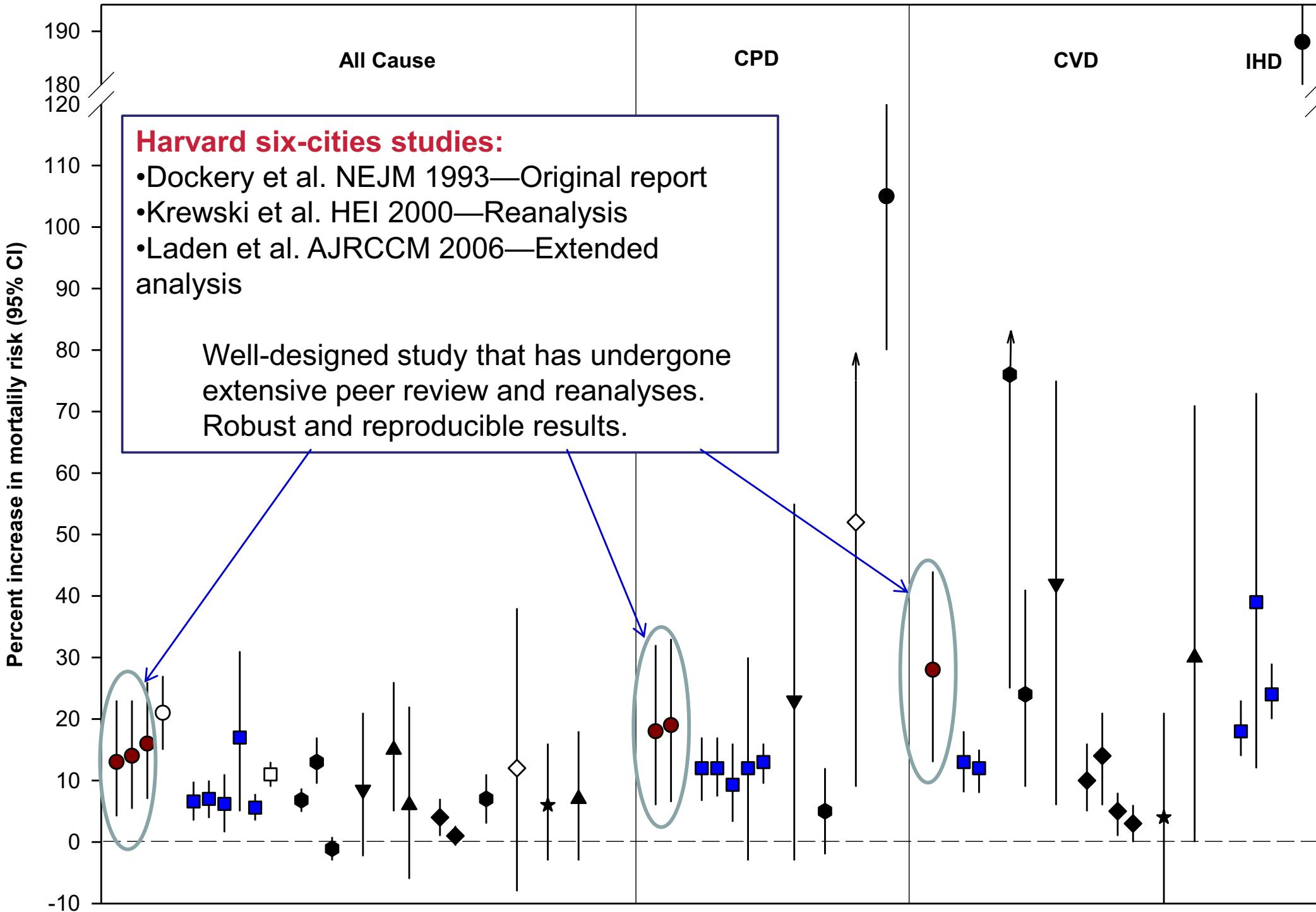


Figure 4. The model-averaged estimated effect of a 10- $\mu\text{g}/\text{m}^3$ increase in PM_{2.5} on all-cause mortality at different lags (in years) between exposure and death. Each lag is estimated independently of the others. Also shown are the pointwise 95% CIs for each lag, based on jackknife estimates.



Particulate Air Pollution as a Predictor of Mortality in a Prospective Study of U.S. Adults



Michael Thun

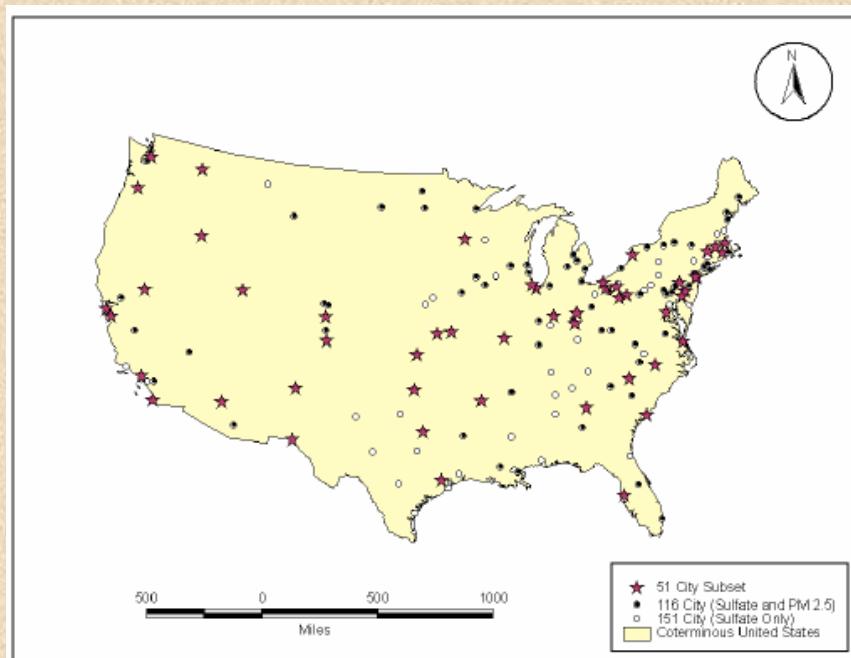
Pope CA III, Thun MJ, Namboodiri MM,
Dockery DW, Evans JS, Speizer FE, Heath CW Jr.



Clark Heath

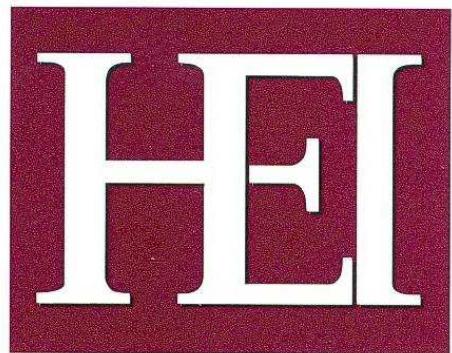


Methods: Linked and analyzed ambient air pollution data from 51-151 U.S. metro areas with risk factor data for over 500,000 adults enrolled in the ACS-CPSII cohort.



Adjusted mortality risk ratios (and 95% CIs) for cigarette smoking the range of sulfates and fine particles

Cause of Death	Current Smoker	Sulfates	Fine Particles
All	2.07 (1.75-2.43)	1.15 (1.09-1.22)	1.17 (1.09-1.26)
Lung Cancer	9.73 (5.96-15.9)	1.36 (1.11-1.66)	1.03 (0.80-1.33)
Cardio-Pulmonary	2.28 (1.79-2.91)	1.26 (1.16-1.37)	1.31 (1.17-1.46)
All other	1.54 (1.19-1.99)	1.01 (0.92-1.11)	1.07 (0.92-1.24)



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SPECIAL REPORT

Reanalysis of the Harvard Six Cities Study and the American Cancer Society Study of Particulate Air Pollution and Mortality

A Special Report of the Institute's Particle Epidemiology Reanalysis Project

Lung Cancer, Cardiopulmonary Mortality, and Long-term Exposure to Fine Particulate Air Pollution

C. Arden Pope III, PhD

Richard T. Burnett, PhD

Michael J. Thun, MD

Eugenia E. Calle, PhD

Daniel Krewski, PhD

Kazuhiko Ito, PhD

George D. Thurston, ScD

Context Associations have been found between day-to-day particulate air and increased risk of various adverse health outcomes, including cardiopulmonary mortality. However, studies of health effects of long-term particulate air pollution have been less conclusive.

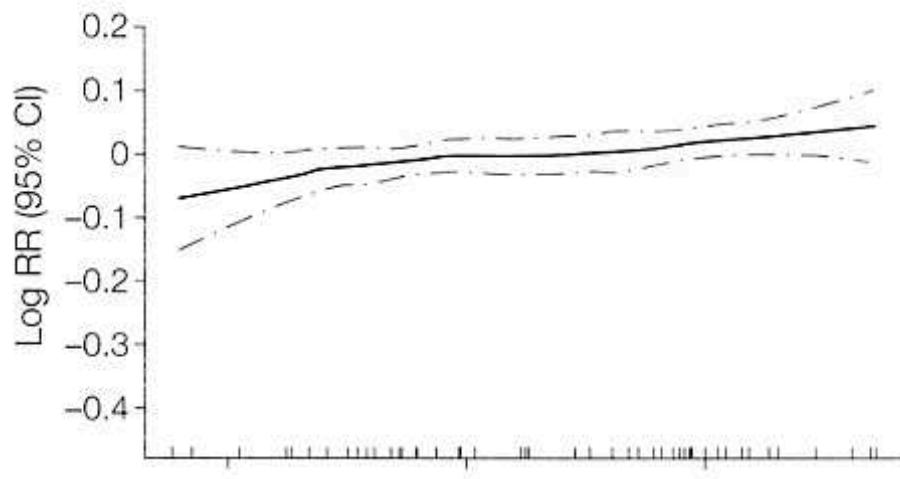
Objective To assess the relationship between long-term exposure to fine particulate air pollution and all-cause, lung cancer, and cardiopulmonary mortality.

Design, Setting, and Participants Vital status and cause of death data were collected by the American Cancer Society as part of the Cancer Prevention II study, a large-scale, ongoing prospective mortality study, which enrolled approximately 1.2 million adults.

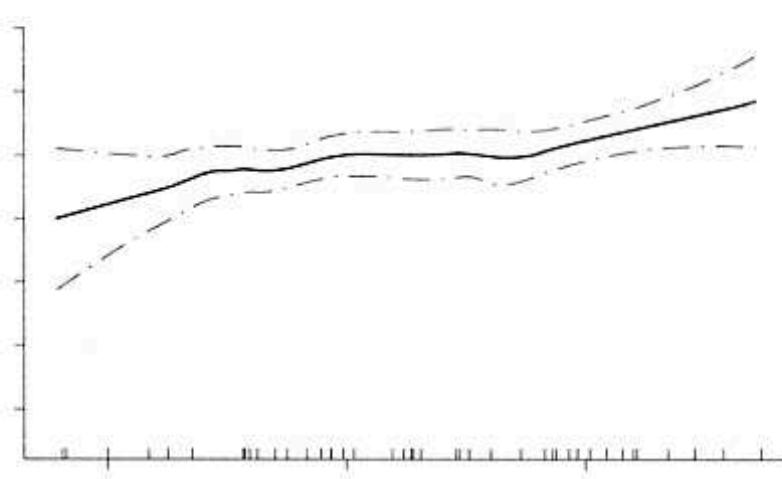


Figure 2. Nonparametric Smoothed Exposure Response Relationship

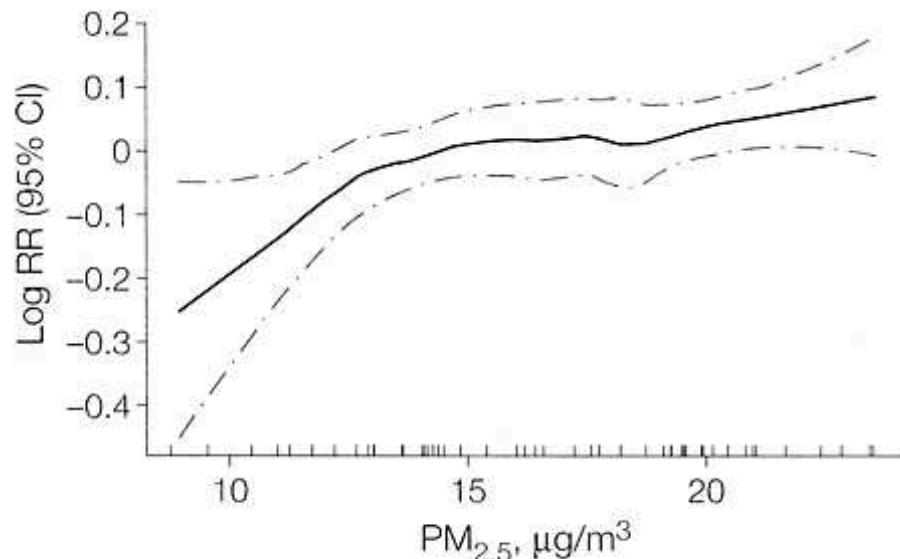
A All-Cause Mortality



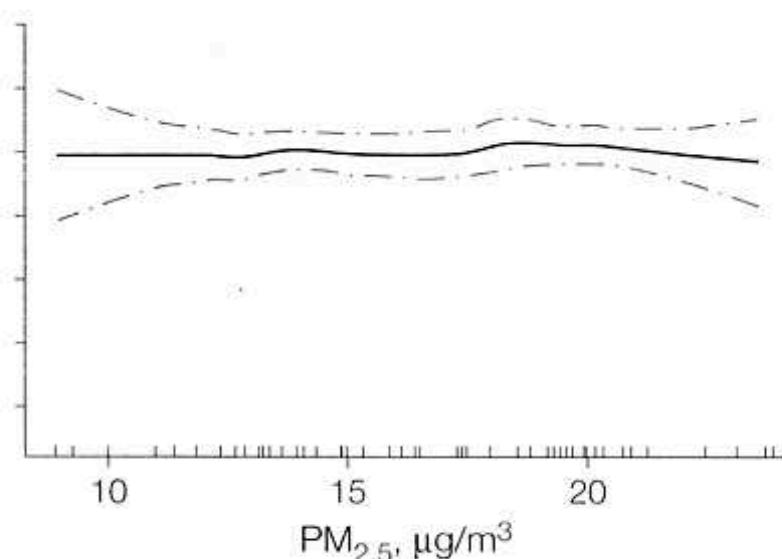
B Cardiopulmonary Mortality



C Lung Cancer Mortality



D All Other Cause Mortality



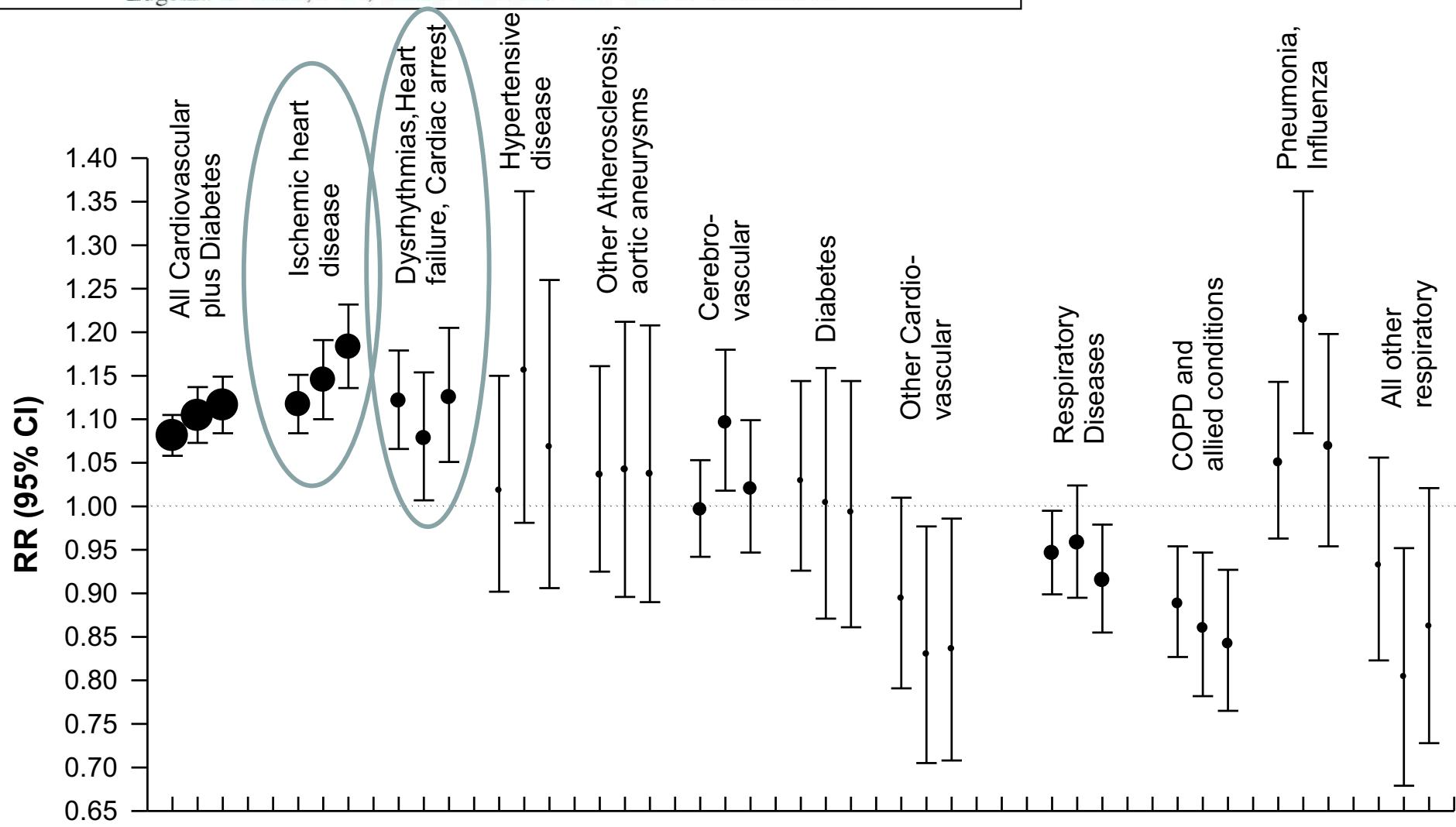
Cardiovascular Mortality and Long-Term Exposure to Particulate Air Pollution

Epidemiological Evidence of General Pathophysiological Pathways of Disease

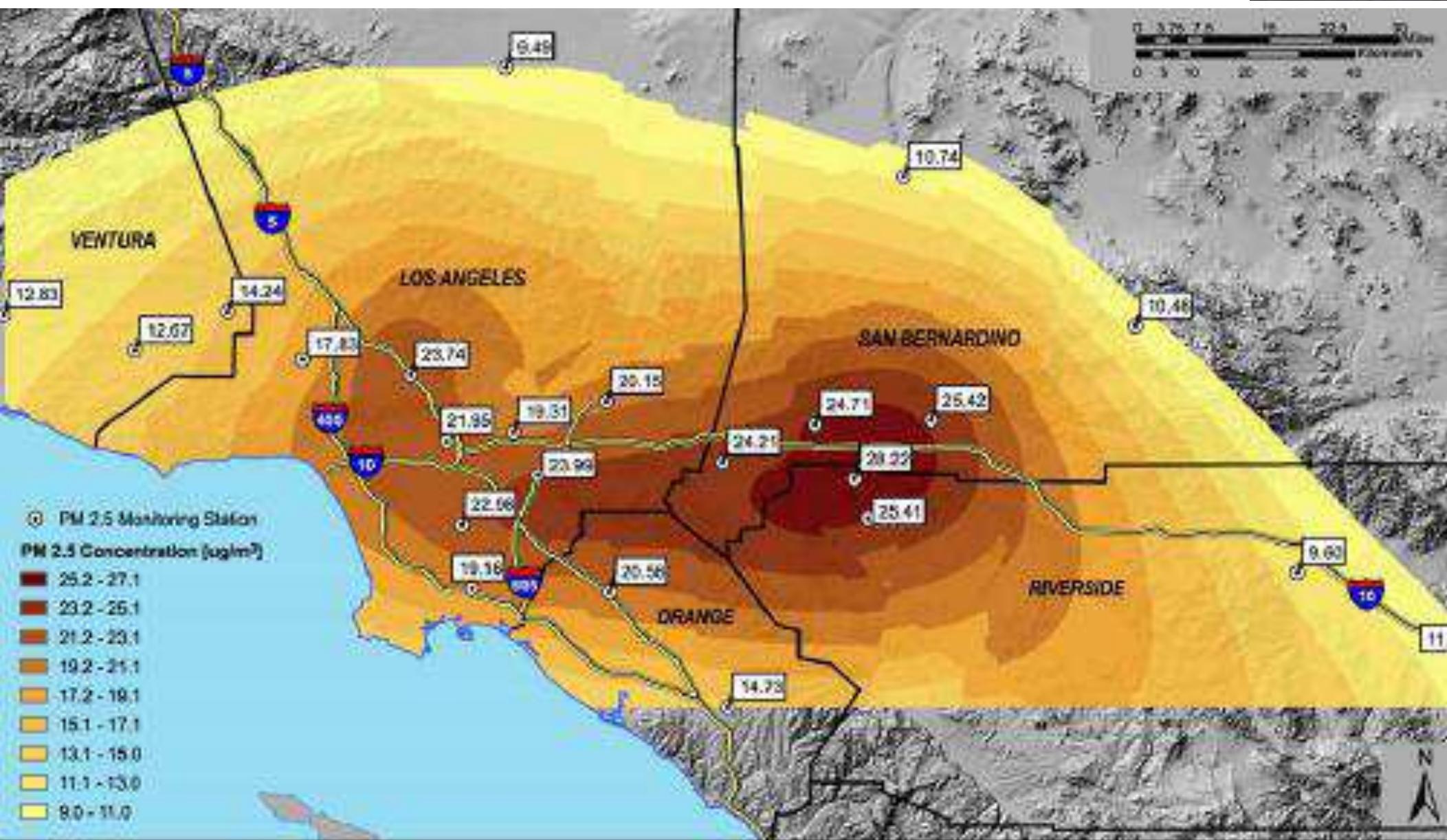
C. Arden Pope III, PhD; Richard T. Burnett, PhD; George D. Thurston, ScD; Michael J. Thun, MD;
Eugenia E. Calle, PhD; Daniel Krewski, PhD; John J. Godleski, MD



John Godleski



Spatial analysis of air pollution and mortality in Los Angeles. (Jerrett, Burnett, Ma, Pope, et al. Epidemiology 2005)



LOS ANGELES

Follow up 1982-2000 Cox Model Covariates	All Cause	Cause of Death		
		IHD ICD9: 410-414	Cardiopulmonary ICD9: 400-440, 460- 519	Lung Cancer ICD9: 162
Total subjects: N=22,905	5,856	1,462	3,136	434
PM2.5 (LUR28pred) only	1.197 (1.082,1.325)	1.415 (1.154,1.735)	1.179 (1.025,1.356)	1.460(1.013,2.105)
44 Individual Covariates	1.143 (1.033,1.266)	1.331 (1.084,1.634)	1.114 (0.968,1.282)	1.392(0.964,2.010)
+ Air Conditioning	1.142 (1.031,1.265)	1.333 (1.085,1.638)	1.121 (0.974,1.290)	1.376(0.952,1.989)
+ Percent of Black	1.145 (1.033,1.269)	1.347 (1.096,1.656)	1.120 (0.972,1.289)	1.411(0.976,2.041)
+ Percent of White	1.151 (1.036,1.278)	1.362 (1.103,1.682)	1.127 (0.976,1.302)	1.471(1.008,2.147)
+ Percent of Hispanic	1.132 (1.016,1.261)	1.322 (1.065,1.641)	1.113 (0.960,1.290)	1.415(0.956,2.096)
+ Percent of Unemployed	1.127 (1.015,1.252)	1.328 (1.075,1.641)	1.129 (0.977,1.305)	1.279(0.879,1.862)
+ Mean Income	1.146 (1.035,1.268)	1.332 (1.086,1.635)	1.115 (0.970,1.283)	1.388(0.963,2.001)
+ Total population	1.141 (1.030,1.264)	1.322 (1.076,1.624)	1.108 (0.963,1.275)	1.396(0.967,2.016)
+ Income inequality	1.110 (0.999,1.234)	1.254 (1.014,1.552)	1.056 (0.913,1.222)	1.306(0.893,1.910)
+ Percent of GRD12	1.144 (1.033,1.266)	1.334 (1.087,1.637)	1.118 (0.972,1.286)	1.386(0.961,2.000)
+ All social factors	1.142 (1.026,1.272)	1.322 (1.064,1.642)	1.107 (0.954,1.285)	1.399(0.949,2.061)
+ AC, Income, GRD12,SF	1.115 (1.003,1.239)	1.263 (1.020,1.563)	1.072 (0.926,1.241)	1.290(0.881,1.890)
+ Parsimonious con. Covs.	1.126 (1.014,1.251)	1.264 (1.022,1.563)	1.086 (0.939,1.256)	1.311(0.897,1.915)
Copollutant control				
44 Covs .+ O3 (EPDC)	1.191 (1.069,1.327)	1.455 (1.171,1.810)	1.187 (1.023,1.378)	1.446(0.982,2.128)
44 Covs. + O3 (Average)	1.176 (1.057,1.307)	1.431 (1.155,1.772)	1.152 (0.996,1.334)	1.489(1.018,2.178)
44 Cvos. + FreeWays	1.170 (1.054,1.299)	1.393 (1.127,1.721)	1.134 (0.982,1.310)	1.439(0.989,2.095)
Copollutant risk estimates				
Ozone (EPDC)	0.985(0.964,1.006)	0.973(0.932,1.015)	0.966 (0.938,0.994)	0.989(0.917,1.068)
Ozone (Average)	0.993(0.977,1.010)	0.984(0.952,1.017)	0.985(0.963,1.008)	0.970(0.912,1.032)
FreeWay within 500 m	0.987(0.875,1.113)	0.898(0.706,1.143)	0.915(0.775,1.081)	1.440(0.939,2.208)
FreeWay within 1000m	0.974(0.894,1.062)	1.048(0.885,1.241)	0.982(0.874,1.104)	0.942(0.685,1.295)

Number 140
May 2009

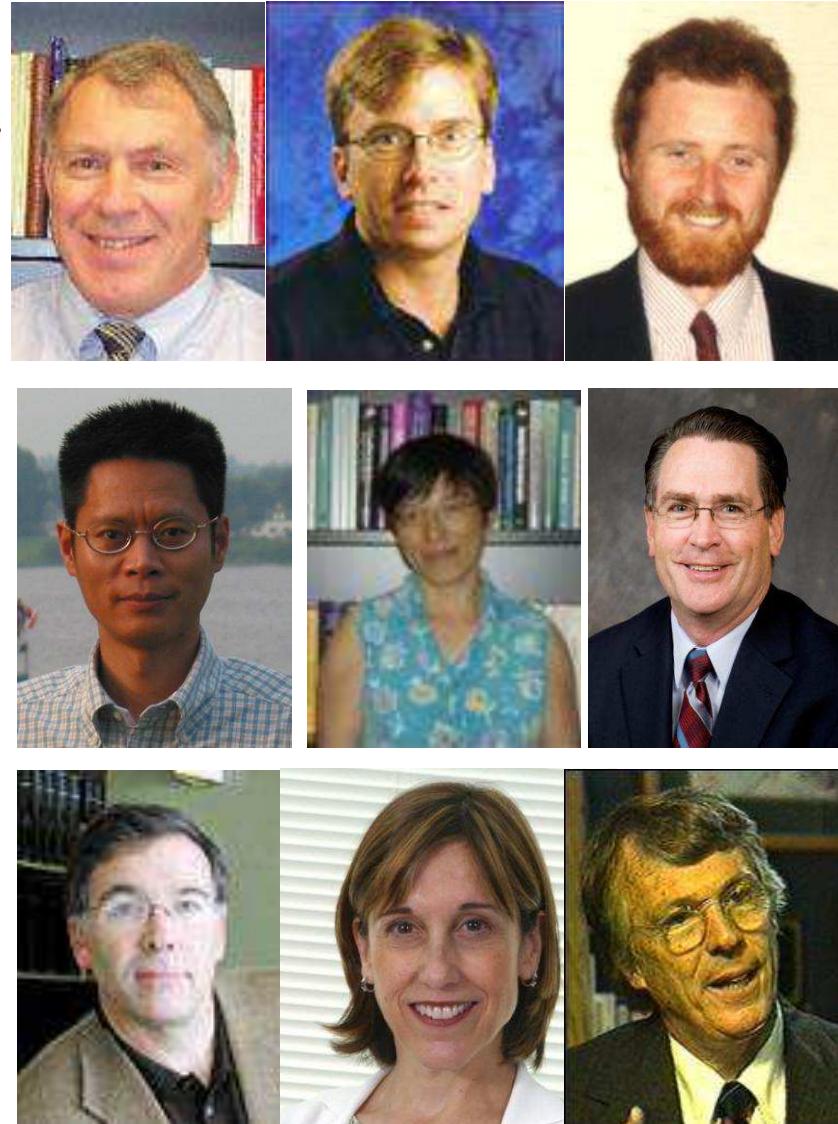
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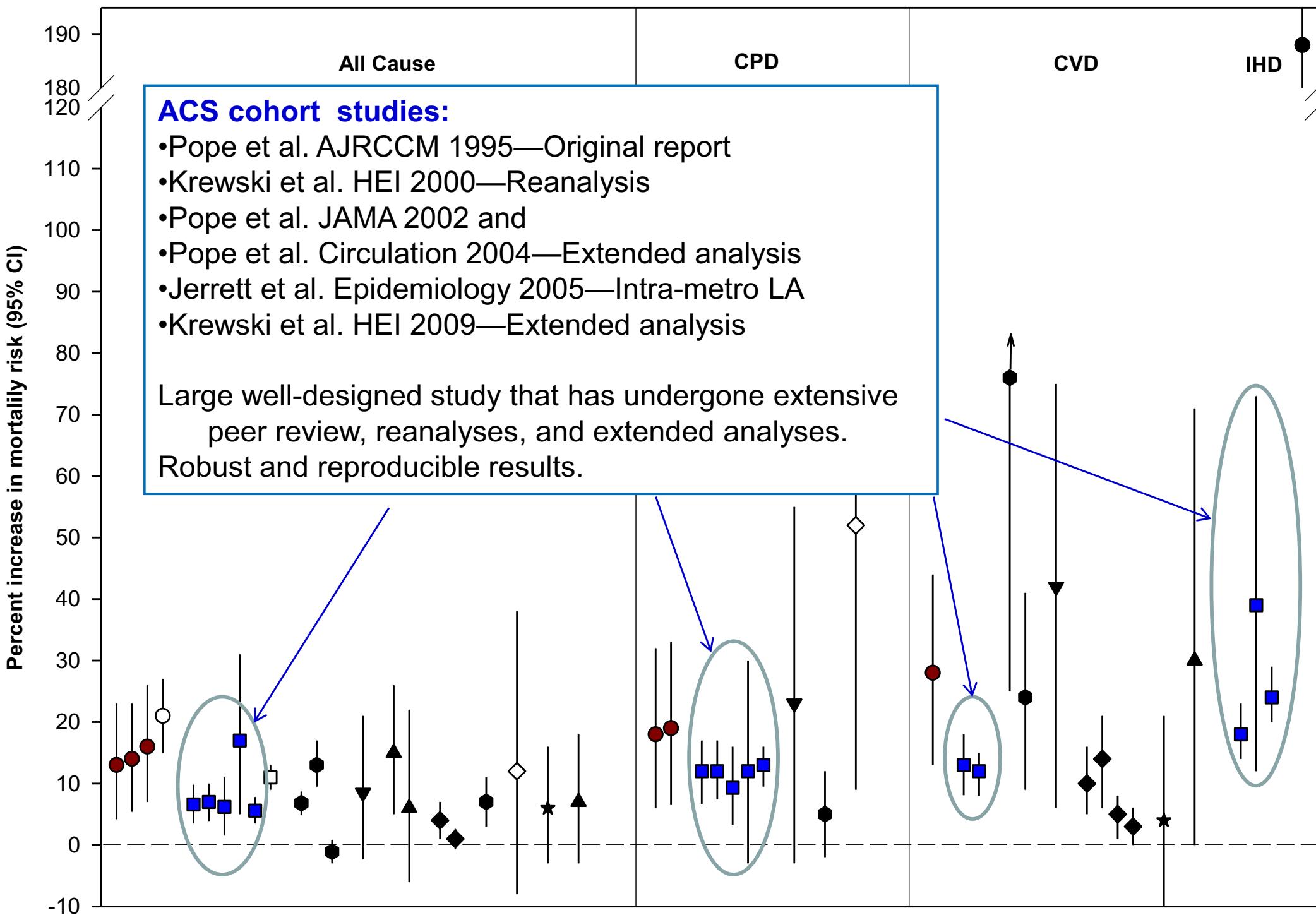
RESEARCH REPORT

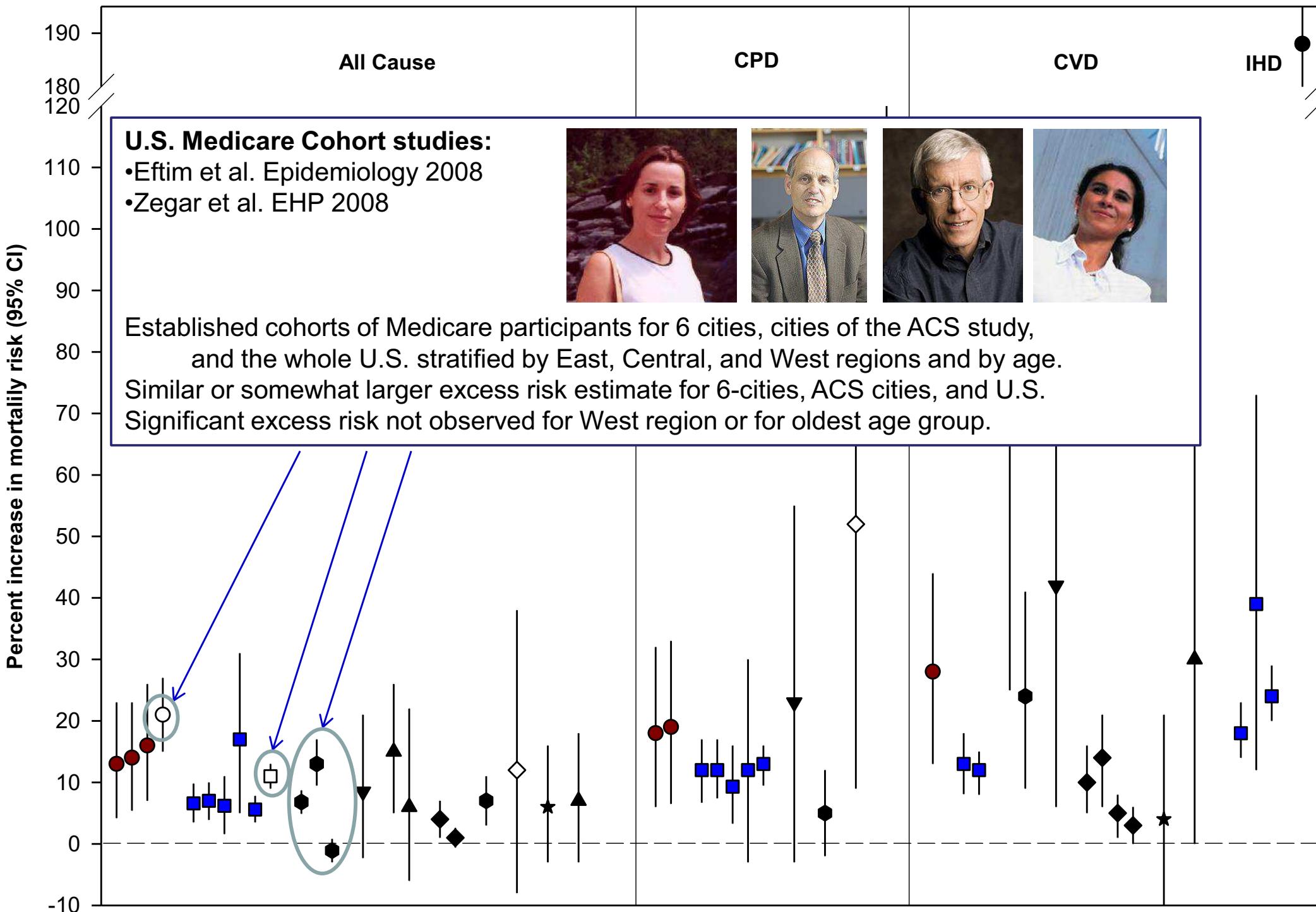
Extended Follow-Up and Spatial Analysis of the American Cancer Society Study Linking Particulate Air Pollution and Mortality

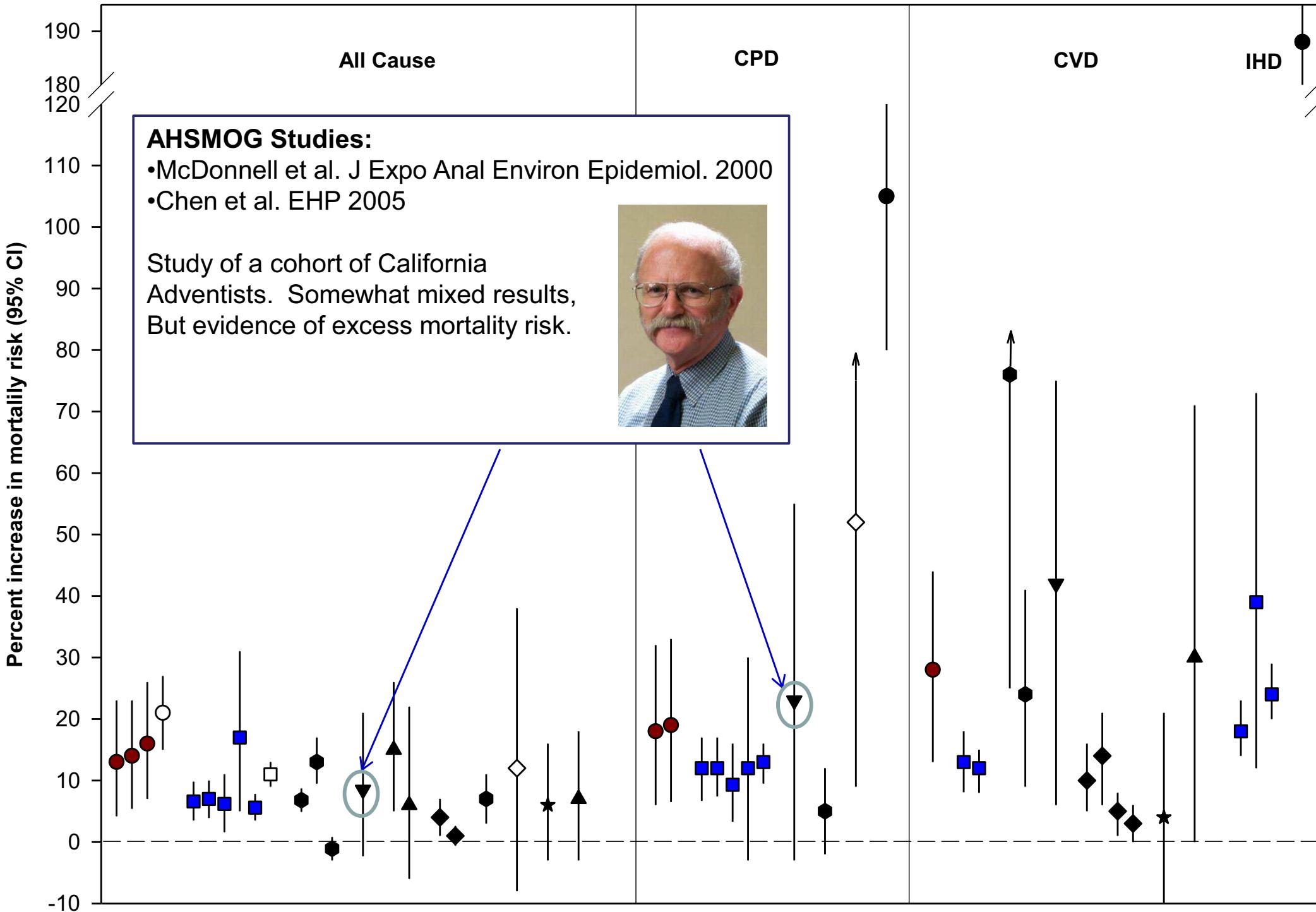
Daniel Krewski, Michael Jerrett, Richard T. Burnett,
Renjun Ma, Edward Hughes, Yuanli Shi,
Michelle C. Turner, C. Arden Pope III, George Thurston,
Eugenia E. Calle, and Michael J. Thun

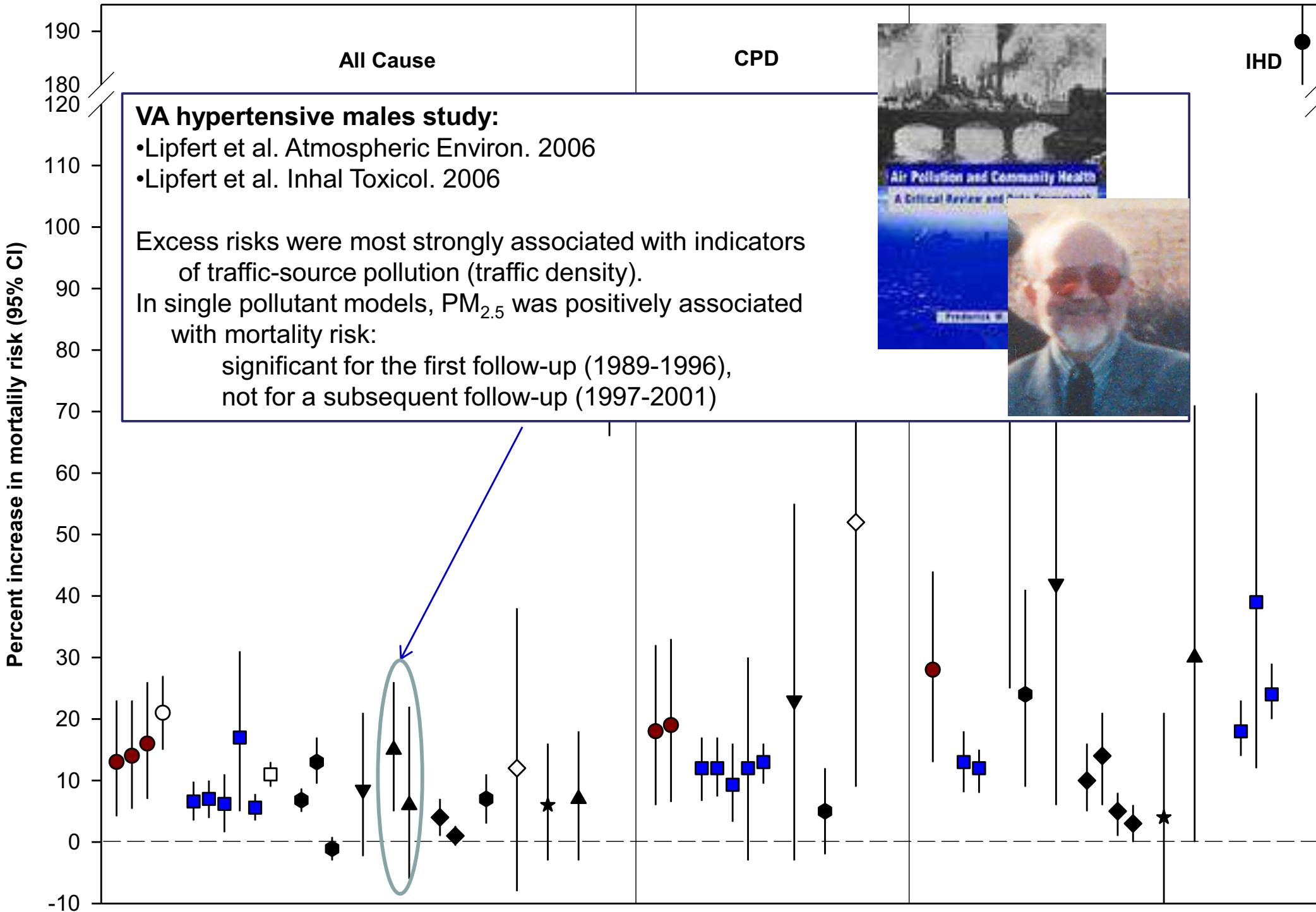
with Bernie Beckerman, Pat DeLuca, Norm Finkelstein,
Kaz Ito, D.K. Moore, K. Bruce Newbold, Tim Ramsay,
Zev Ross, Hwashin Shin, and Barbara Tempalski

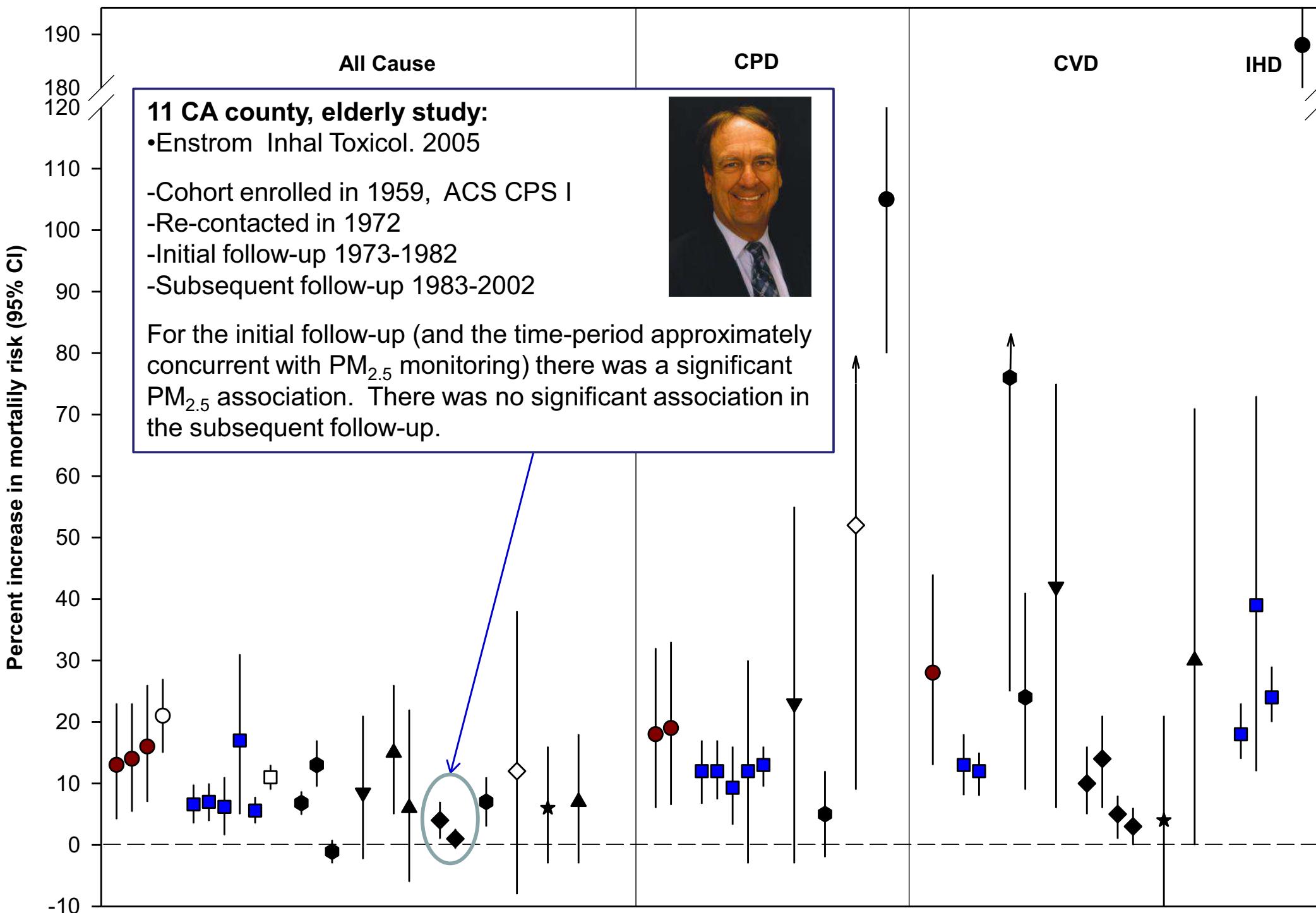


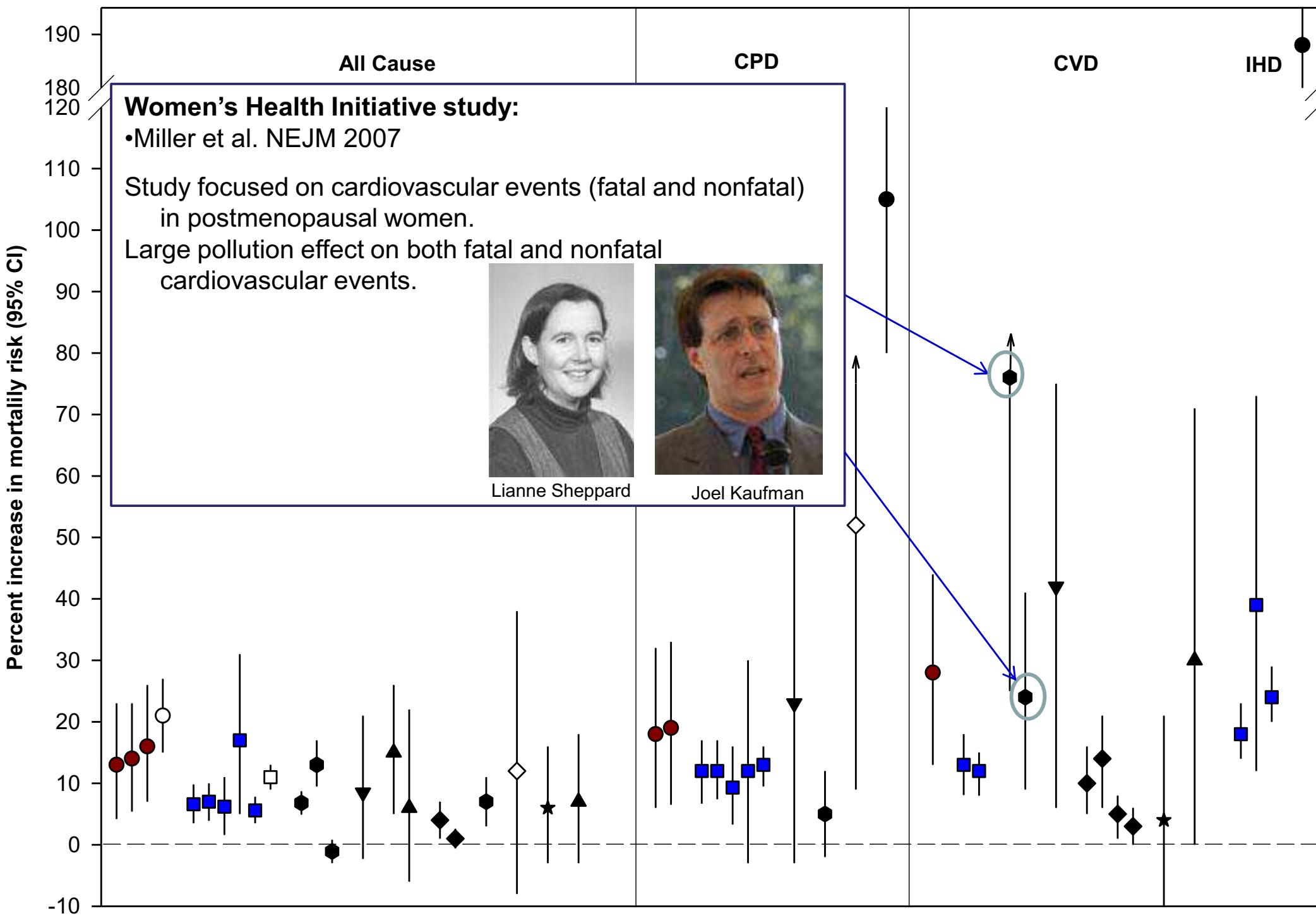


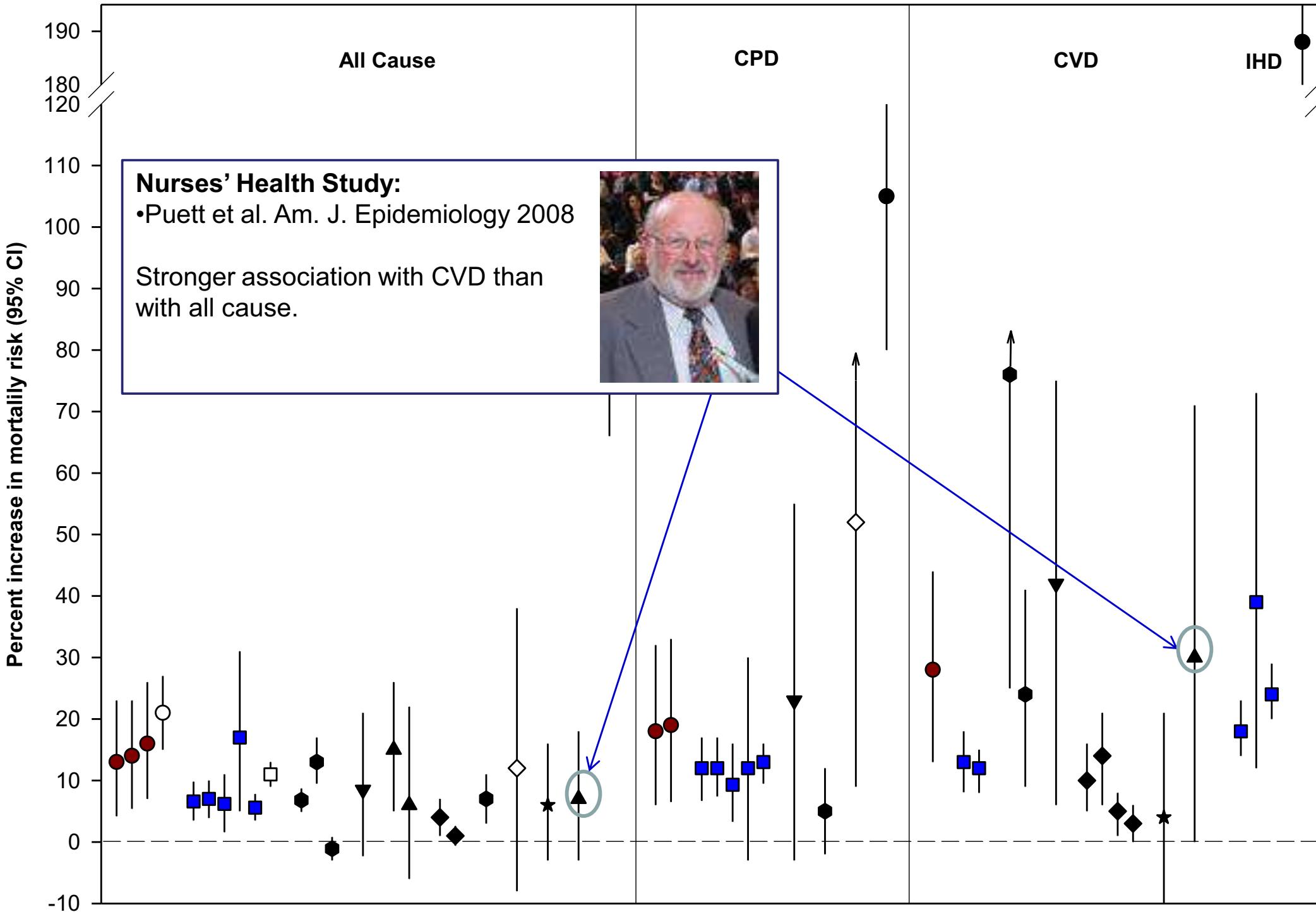


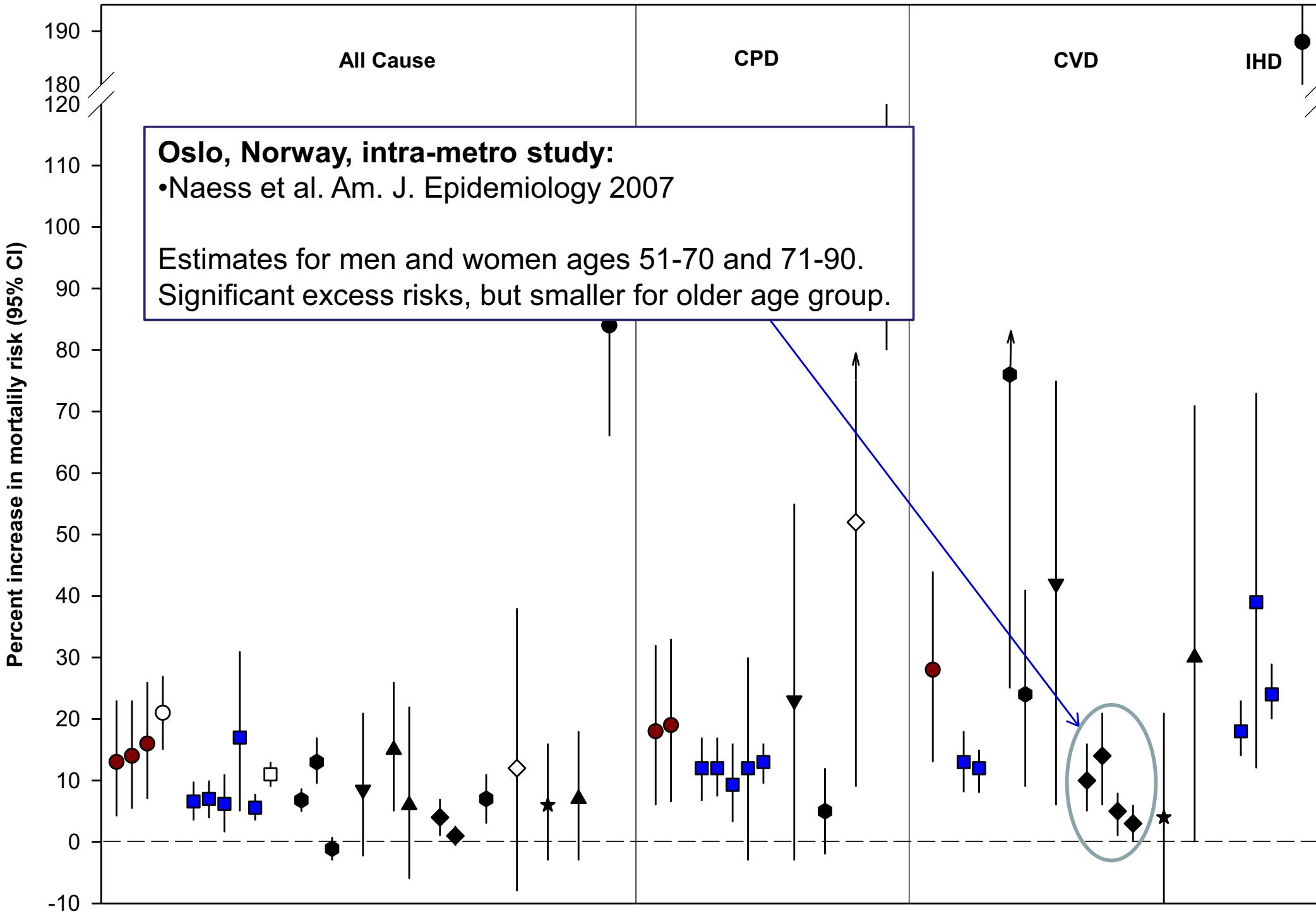










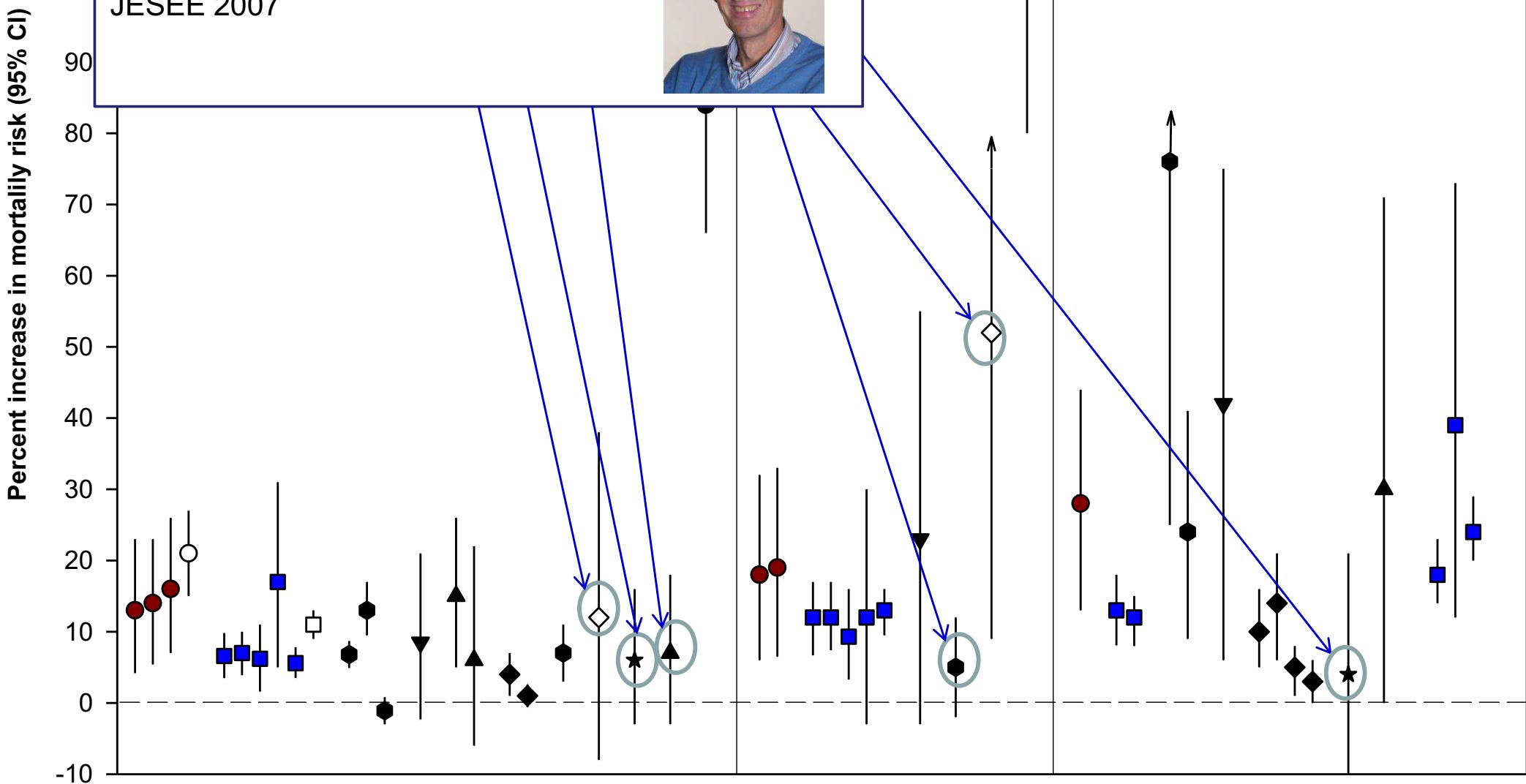


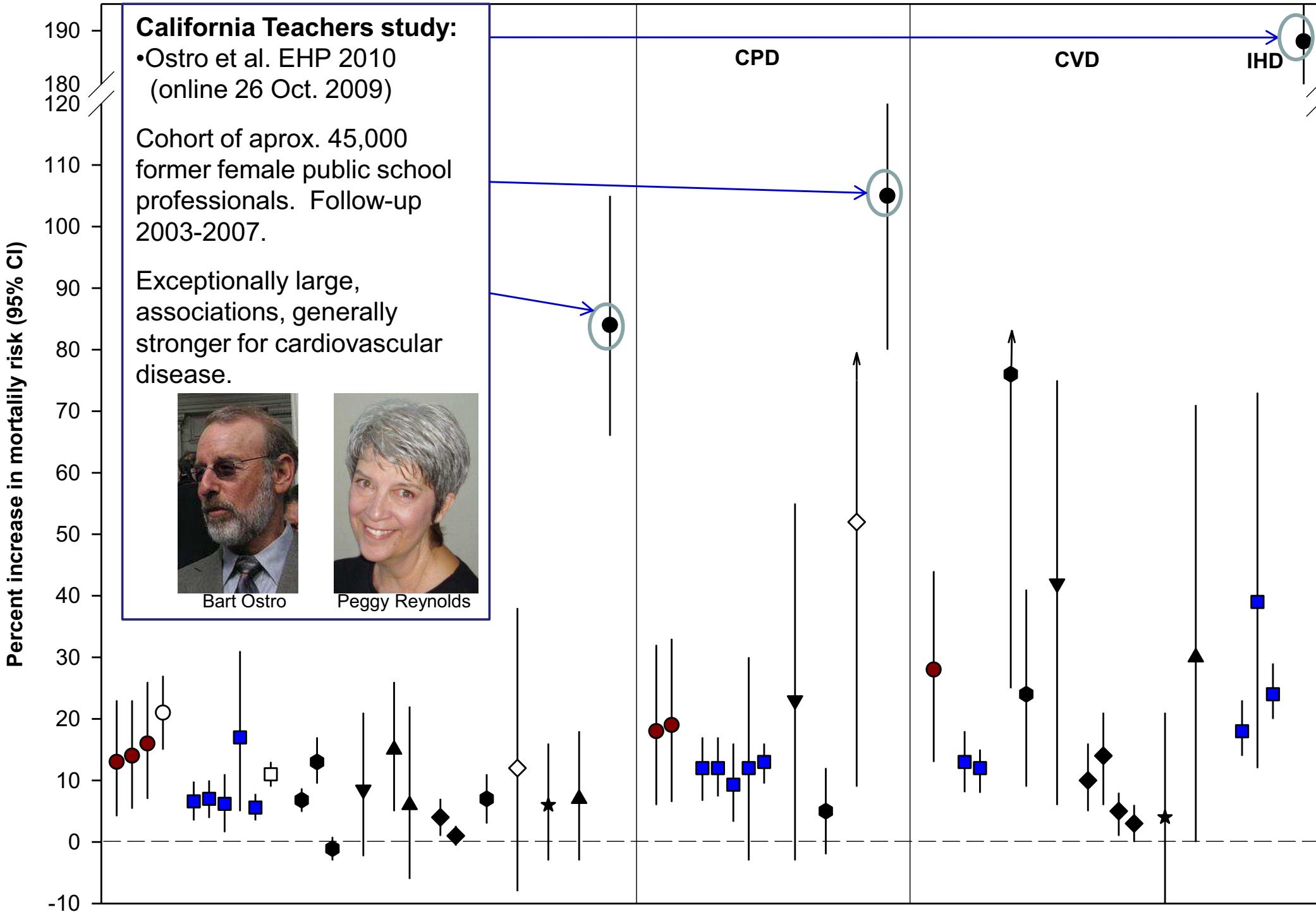
Dutch, French, and German women studies:

- Beelen et al. EHP 2008
- Filleul et al. OEM 2005
- Gehring et al. Epidemiology 2006

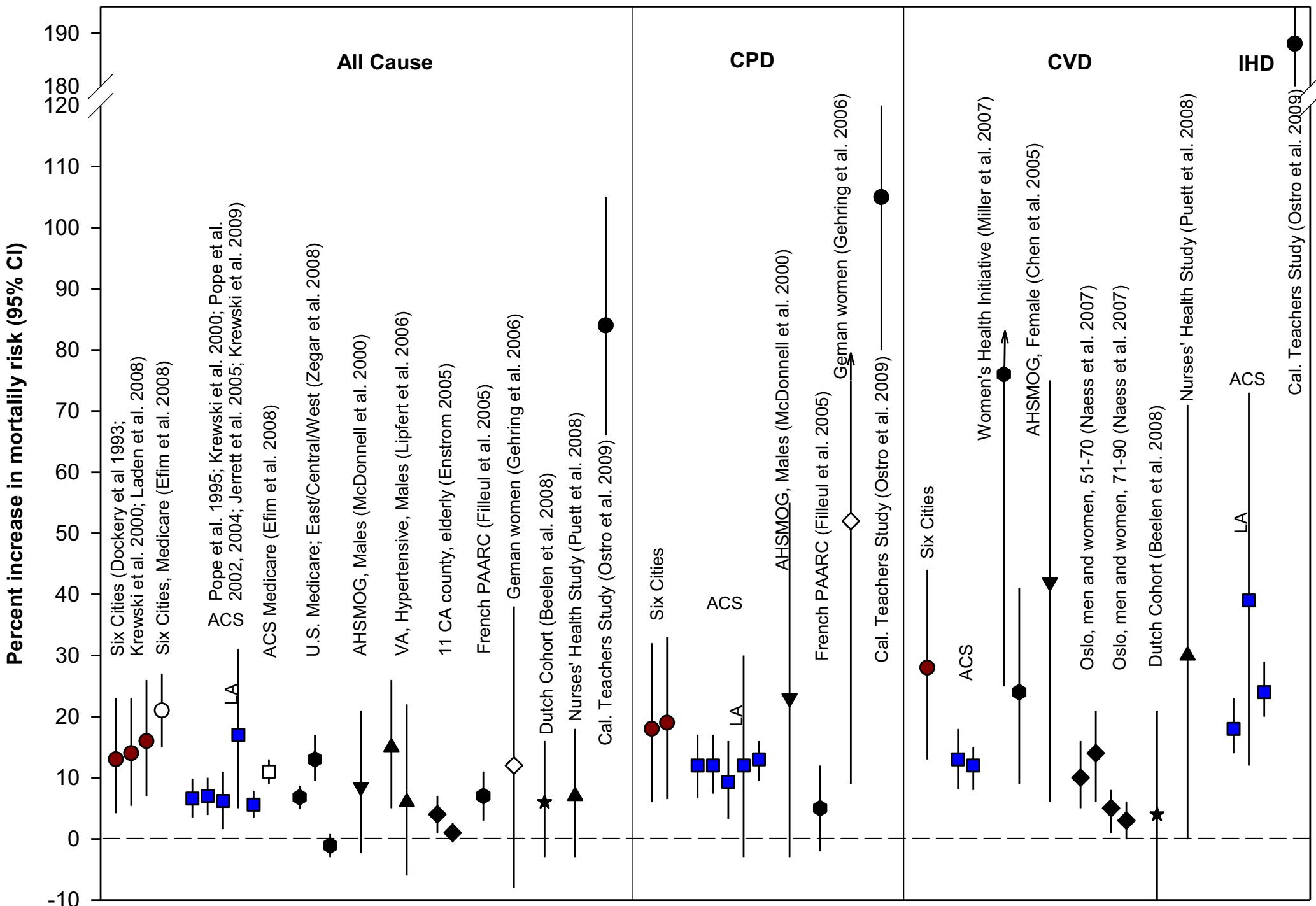
Again, positive associations, generally stronger for cardiovascular disease.

Brunekreef (summary paper)
JESEE 2007





Summary of published cohort and related studies of long-term fine PM exposure. Percent increases in mortality and related risk (95% CIs) associated with $10 \mu\text{g}/\text{m}^3 \text{PM}_{2.5}$ (or other as indicated).



Expert Judgment Assessment of the Mortality Impact of Changes in Ambient Fine Particulate Matter in the U.S. Roman et al. 2008.

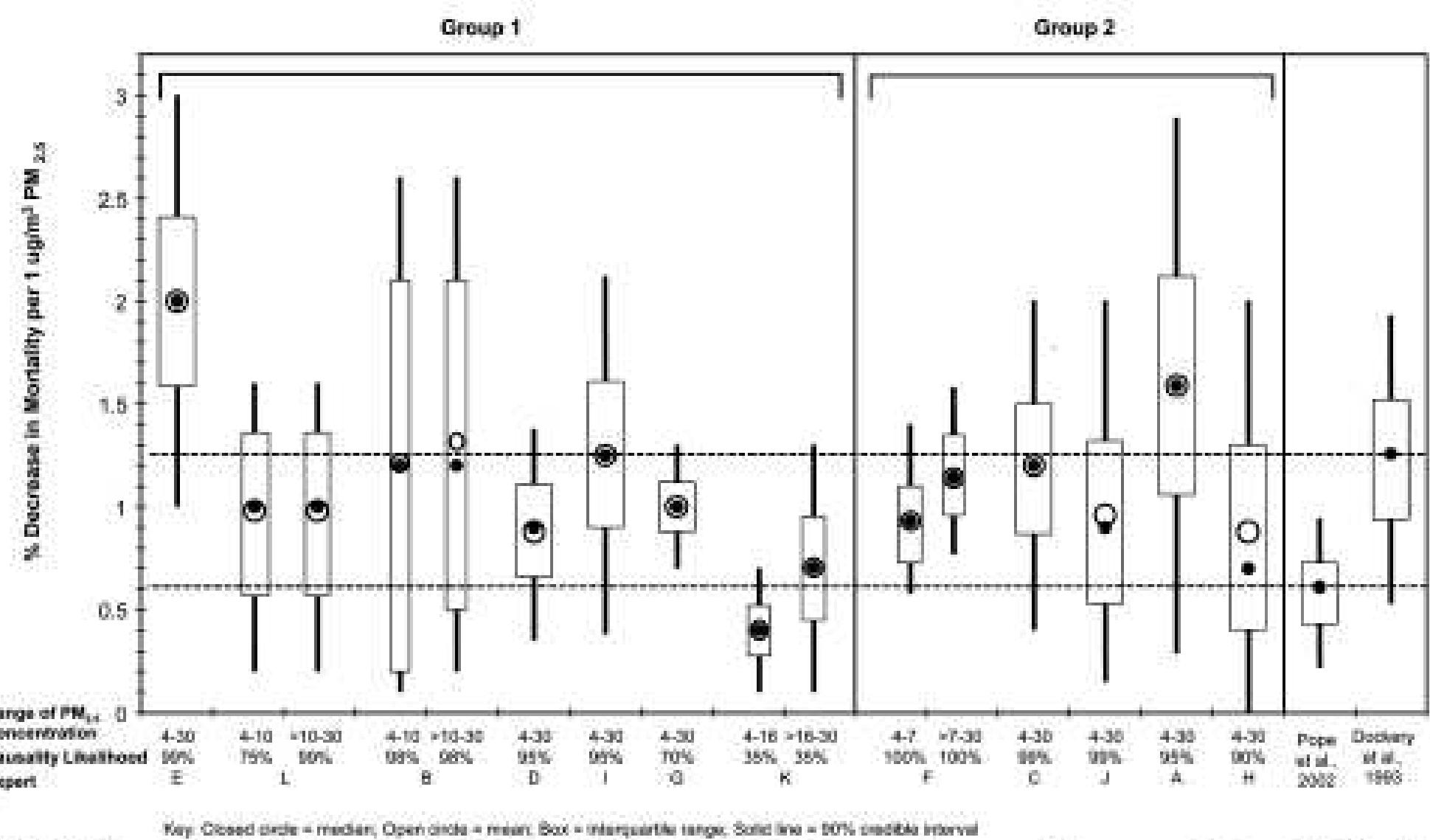


FIGURE 3. Uncertainty distributions for the $\text{PM}_{2.5}$ -mortality C-R coefficient for annual average $\text{PM}_{2.5}$ concentrations of $4\text{--}30 \text{ }\mu\text{g/m}^3$.
 Note: Box plots represent distributions as provided by the experts to the elicitation team. Experts in group 1 preferred to give conditional distributions and keep their probabilistic judgment about the likelihood of a causal or noncausal relationship separate. Experts in group 2 preferred to give distributions that incorporate their likelihood that the $\text{PM}_{2.5}$ -mortality association may be noncausal. Therefore, the expert distributions from these two groups are not directly comparable.

Expert Judgment Assessment of the Mortality Impact of Changes in Ambient Fine Particulate Matter in the U.S. Roman et al. 2008.

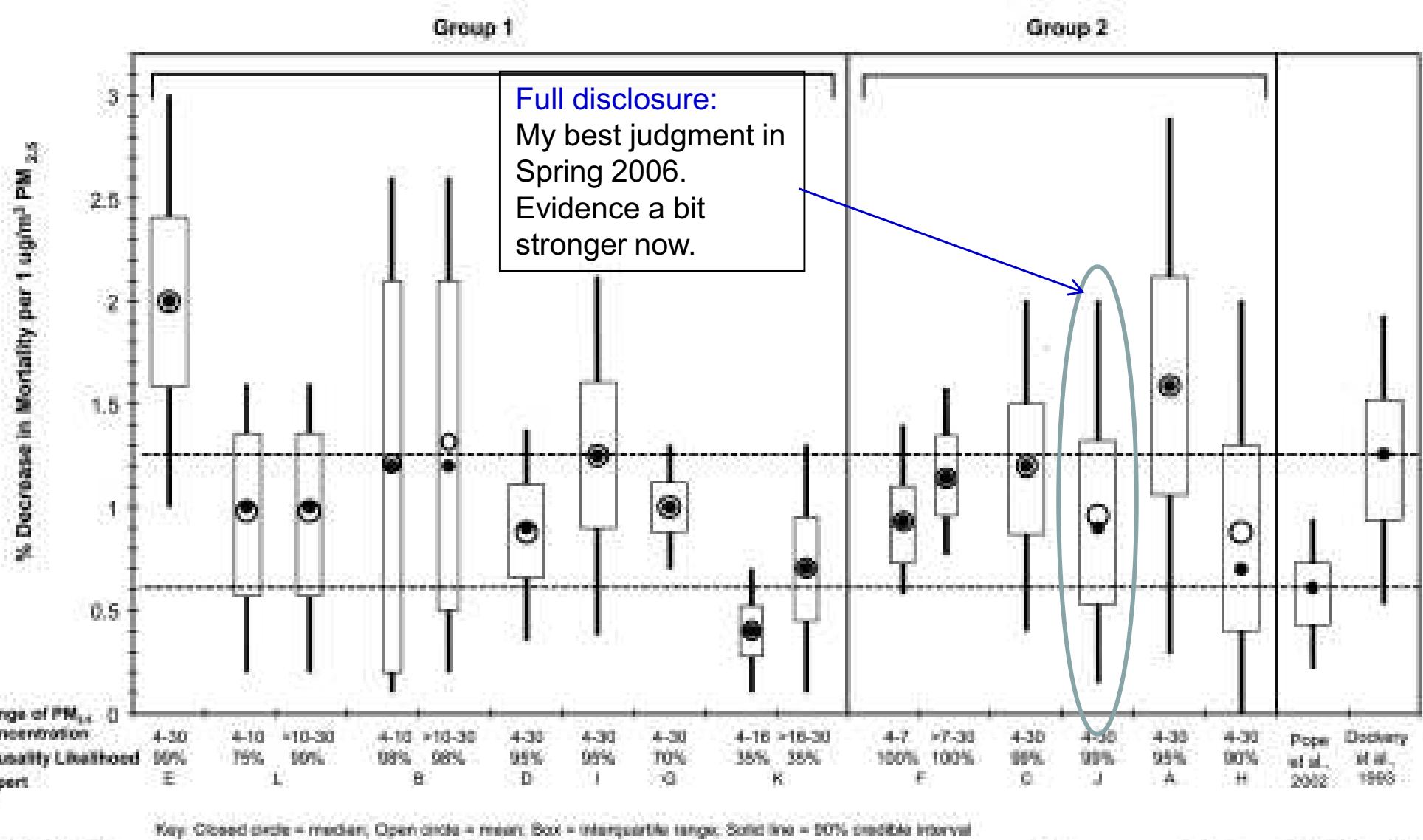
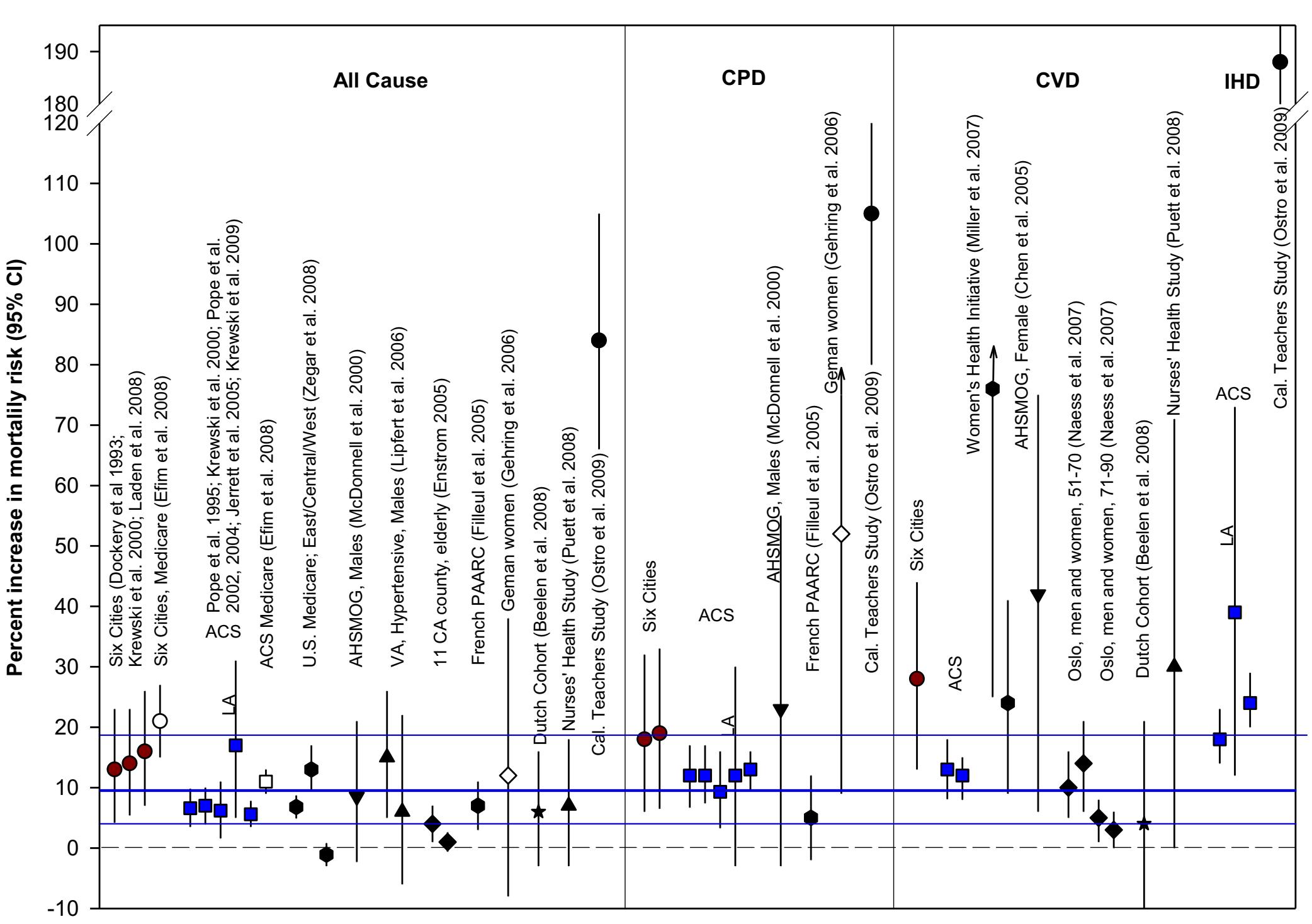


FIGURE 3. Uncertainty distributions for the $\text{PM}_{2.5}$ -mortality C-R coefficient for annual average $\text{PM}_{2.5}$ concentrations of 4–30 $\mu\text{g}/\text{m}^3$.
 Note: Box plots represent distributions as provided by the experts to the elicitation team. Experts in group 1 preferred to give conditional distributions and keep their probabilistic judgment about the likelihood of a causal or noncausal relationship separate. Experts in group 2 preferred to give distributions that incorporate their likelihood that the $\text{PM}_{2.5}$ -mortality association may be noncausal. Therefore, the expert distributions from these two groups are not directly comparable.



So what do we learn from these studies?

1. The predominant statistical inference is that long-term exposure to elevated levels of PM_{2.5} is associated with elevated risk of mortality.
2. Reasonable central effect estimates range from approximately 5-15% increased mortality risk per 10 µg/m³ long-term elevated PM_{2.5} exposure.
3. In general, PM_{2.5} exposure is more strongly associated with cardiovascular-related mortality.
4. There is evidence that the PM_{2.5}-related excess relative risk is smaller for older populations and declines as cohorts age with longer follow-up.

Which studies are appropriate to use to estimate PM_{2.5}-Related Mortality in California?

C. Arden Pope III, PhD

Mary Lou Fulton Professor
Brigham Young University

Presented at: ARB Symposium

Methodology for Estimating Premature Deaths from PM2.5 Exposure
Sacramento, CA
February 26, 2010



Sun QH Lippmann M

Sun et al. (*JAMA* 2005)



Nm3660
apoE^{-/-} mouse

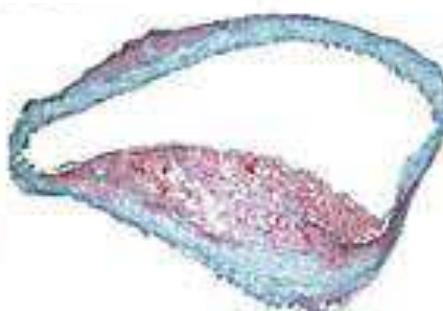
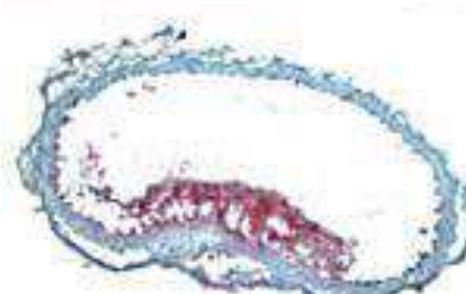
Representative Photomicrographs of Aortic Arch Sections

Normal Chow

Clean
Filtered Air



PM Polluted Air

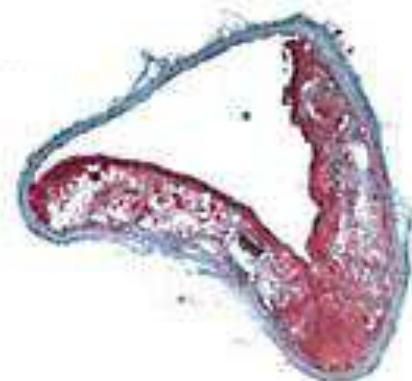
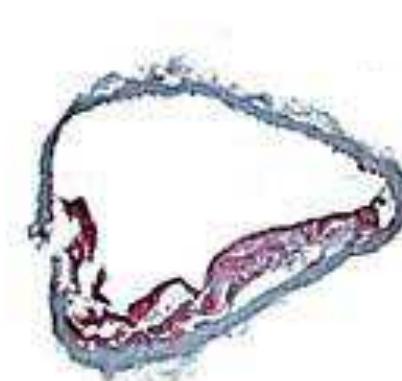
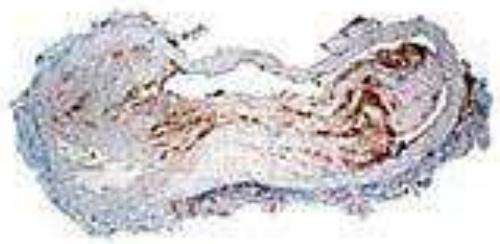
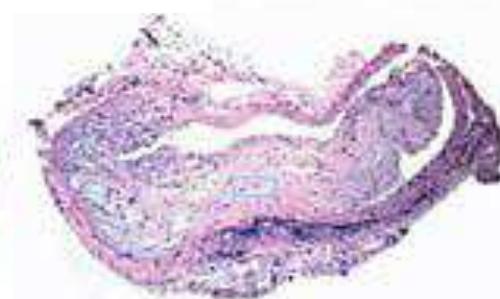


High-Fat Chow

Clean
Filtered Air



PM Polluted Air





Jeffrey Anderson

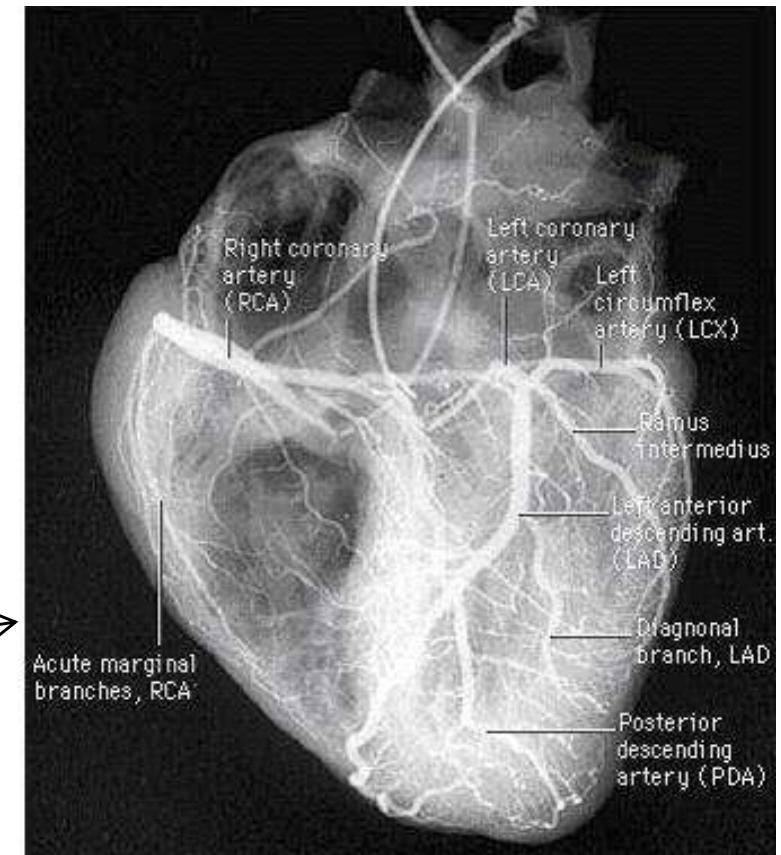
Ischemic Heart Disease Events Triggered by Short-Term Exposure to Fine Particulate Air Pollution

C. Arden Pope III, PhD; Joseph B. Muhlestein, MD; Heidi T. May, MSPH; Dale G. Renlund, MD; Jeffrey L. Anderson, MD; Benjamin D. Horne, PhD, MPH

Methods:

Case-crossover study of acute ischemic coronary events (heart attacks and unstable angina) in 12,865 well-defined and followed up cardiac patients who lived on Utah's Wasatch Front

...and who underwent coronary angiography



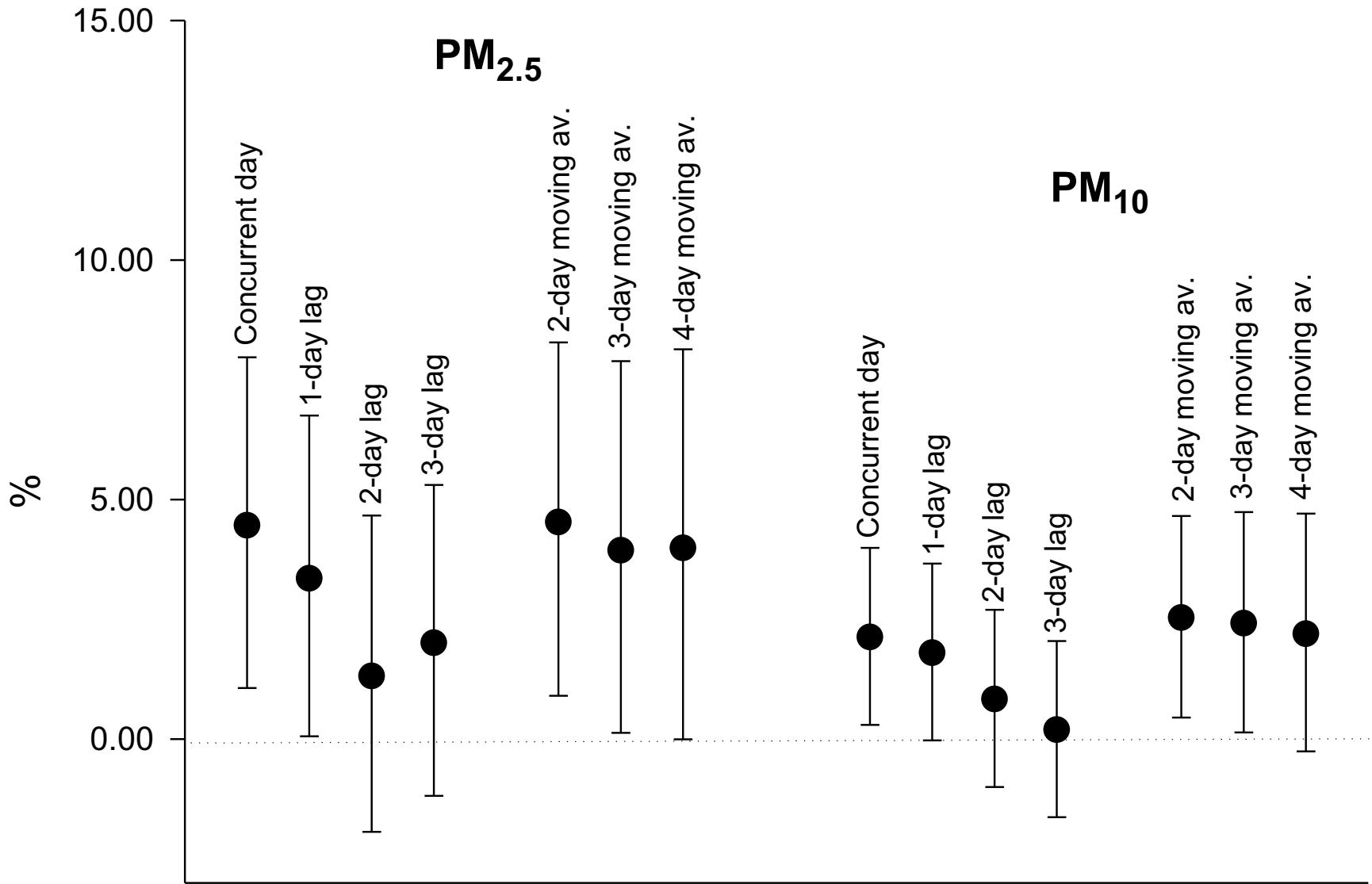


Figure 1. Percent increase in risk (and 95% CI) of acute coronary events associated with $10 \mu\text{g}/\text{m}^3$ of $\text{PM}_{2.5}$, or PM_{10} for different lag structures.

Short-term PM exposures contributed to acute coronary events, especially among patients with underlying coronary artery disease.

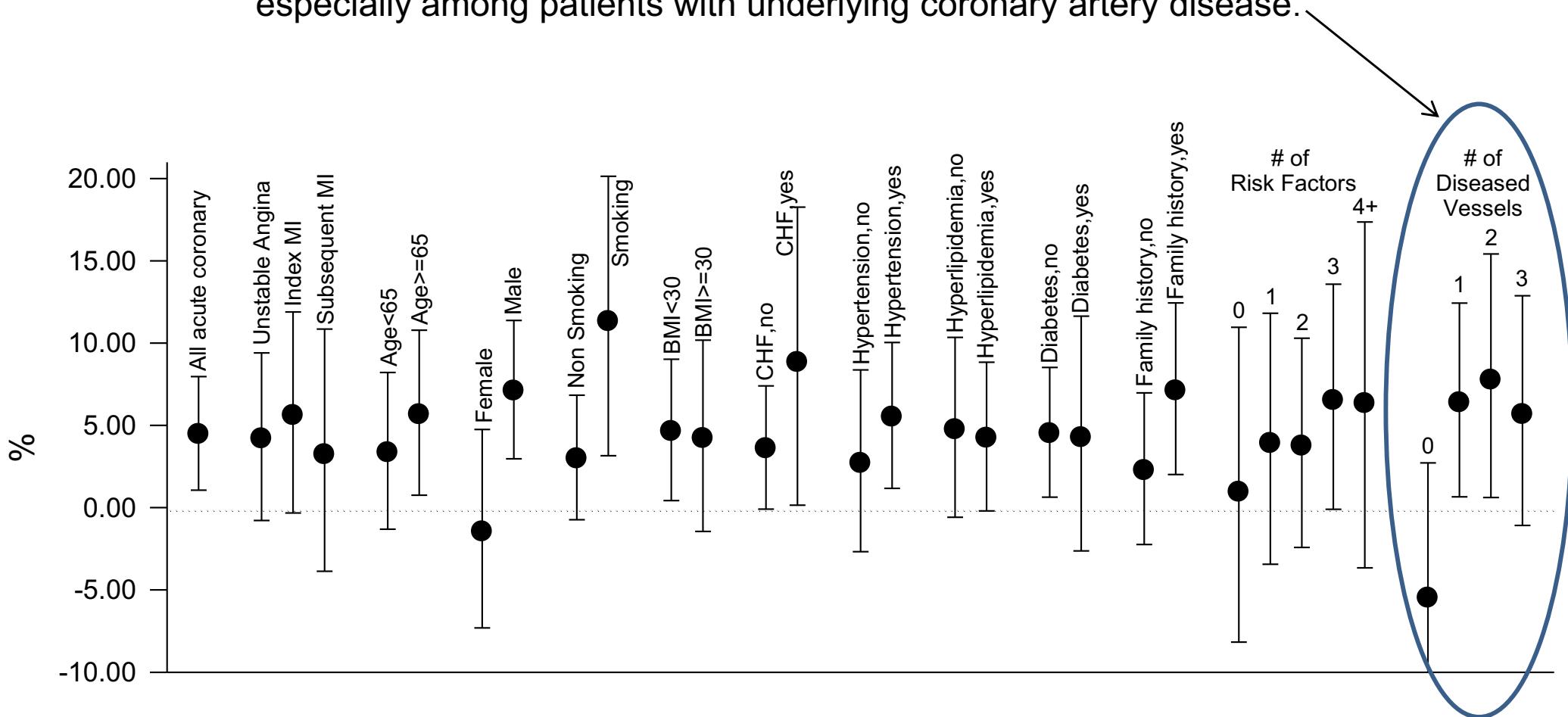
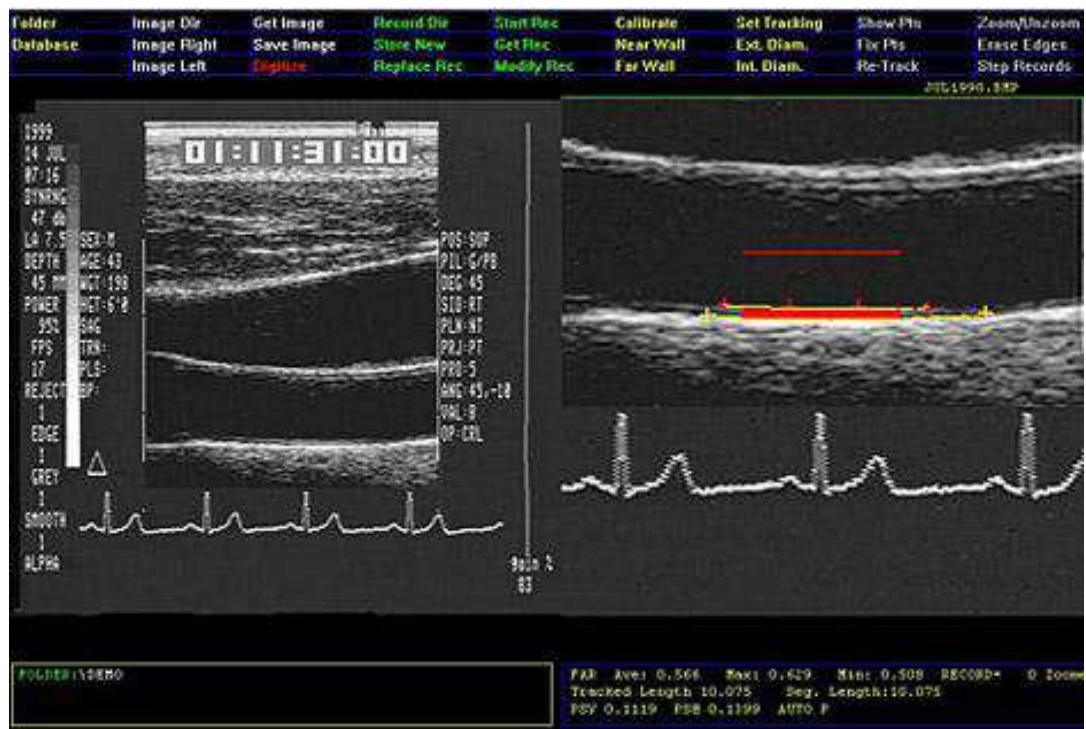


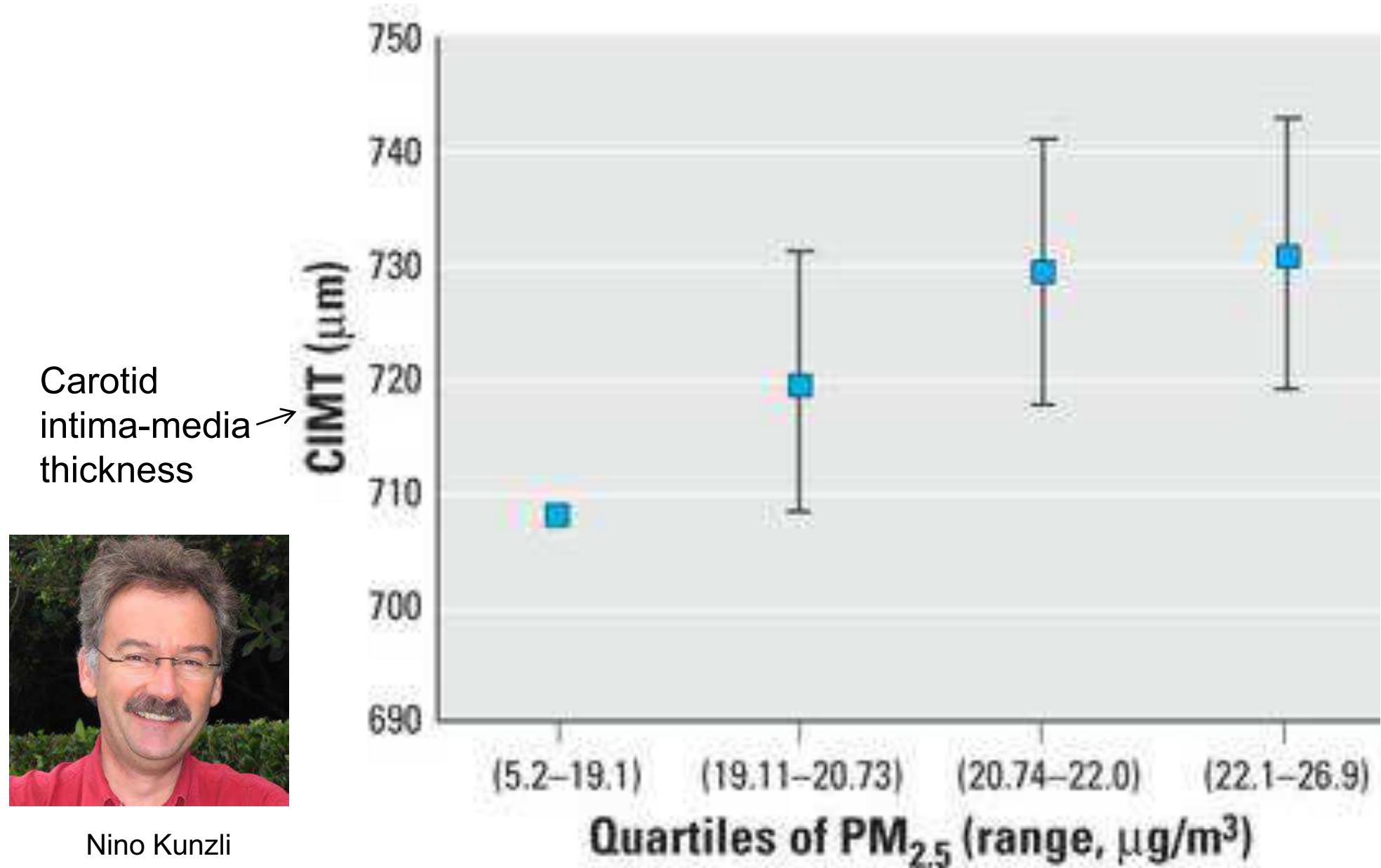
Figure 2. Percent increase in risk (and 95% CI) of acute coronary events associated with $10 \mu\text{g}/\text{m}^3$ of $\text{PM}_{2.5}$, stratified by various characteristics.



Corotid ultrasound to measure carotid intima-media thickness (CIMT).

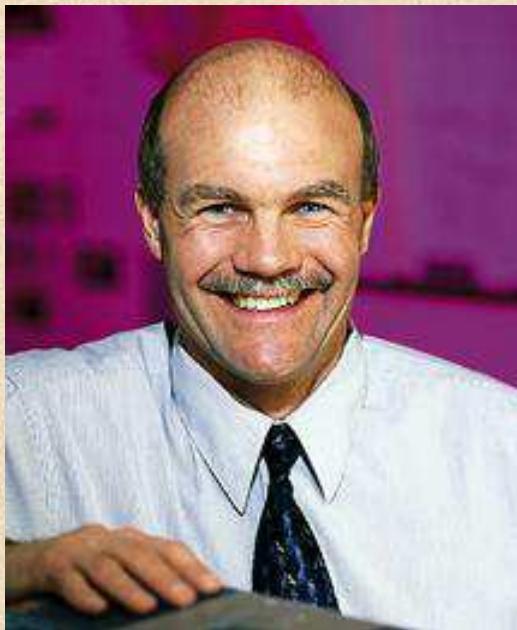
Safe, non-invasive technique to evaluate the burden of subclinical vascular (atherosclerotic) disease.

Ambient Air Pollution and Atherosclerosis in Los Angeles. Kunzli et al. *EHP* 2005.



Southern California Children's Health Study

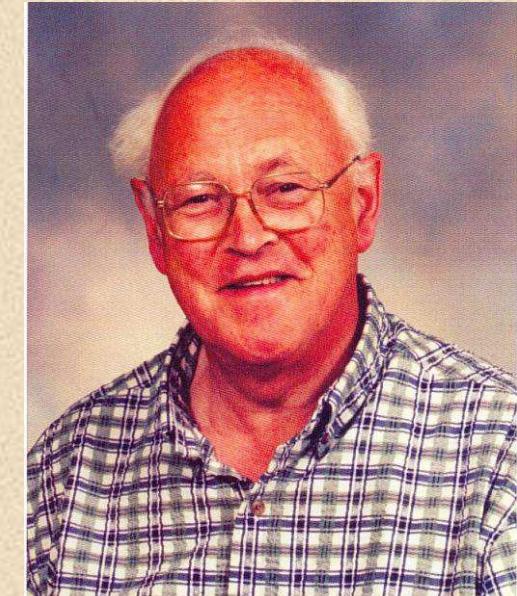
Effects of air pollution on children's health, especially lung function growth.



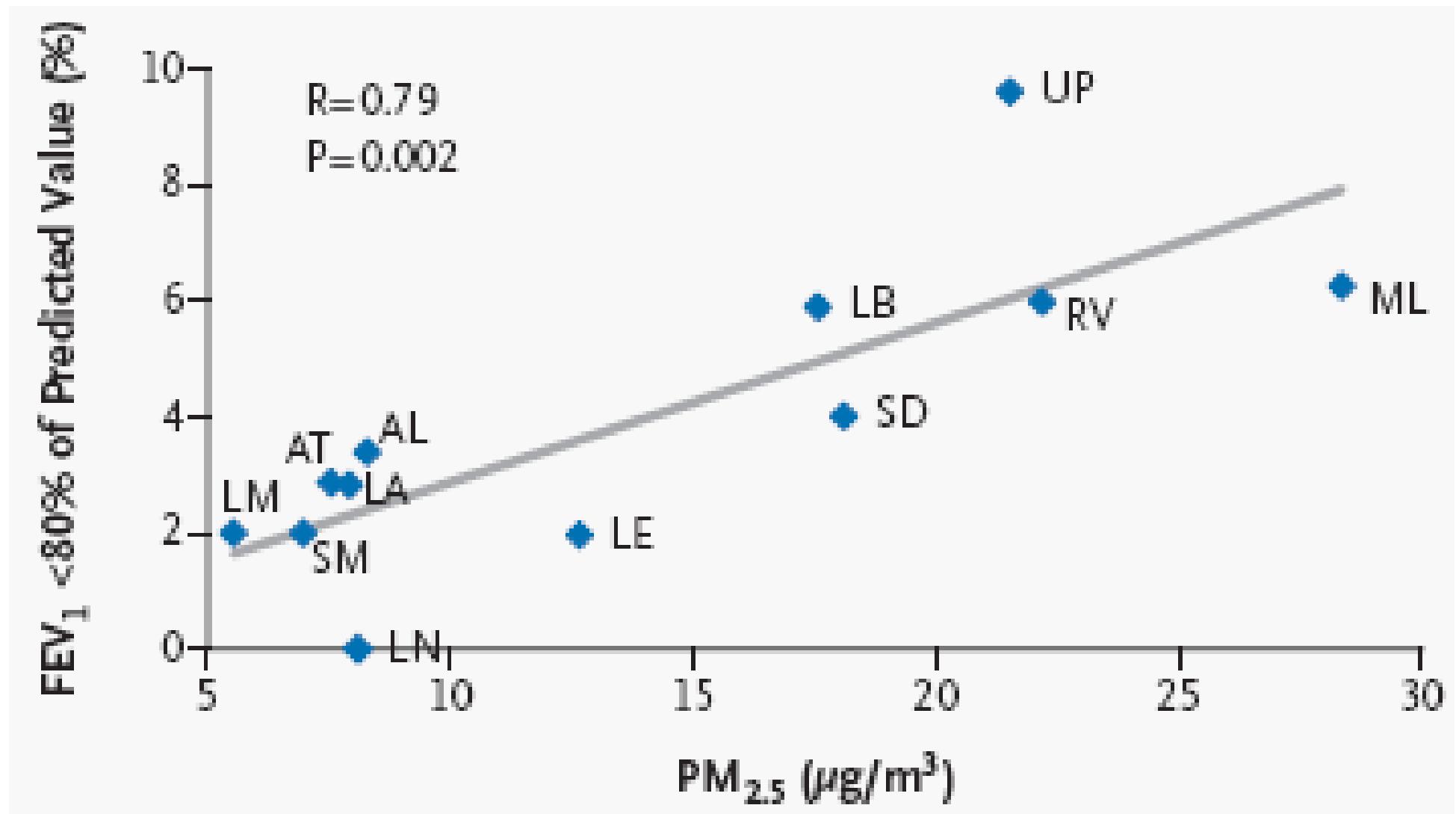
W. James Gauderman



John Peters



David Bates, Advisor



Gauderman et al. The effect of air pollution on lung development from 10 to 18 years of age. *New England Journal of Medicine* 2004

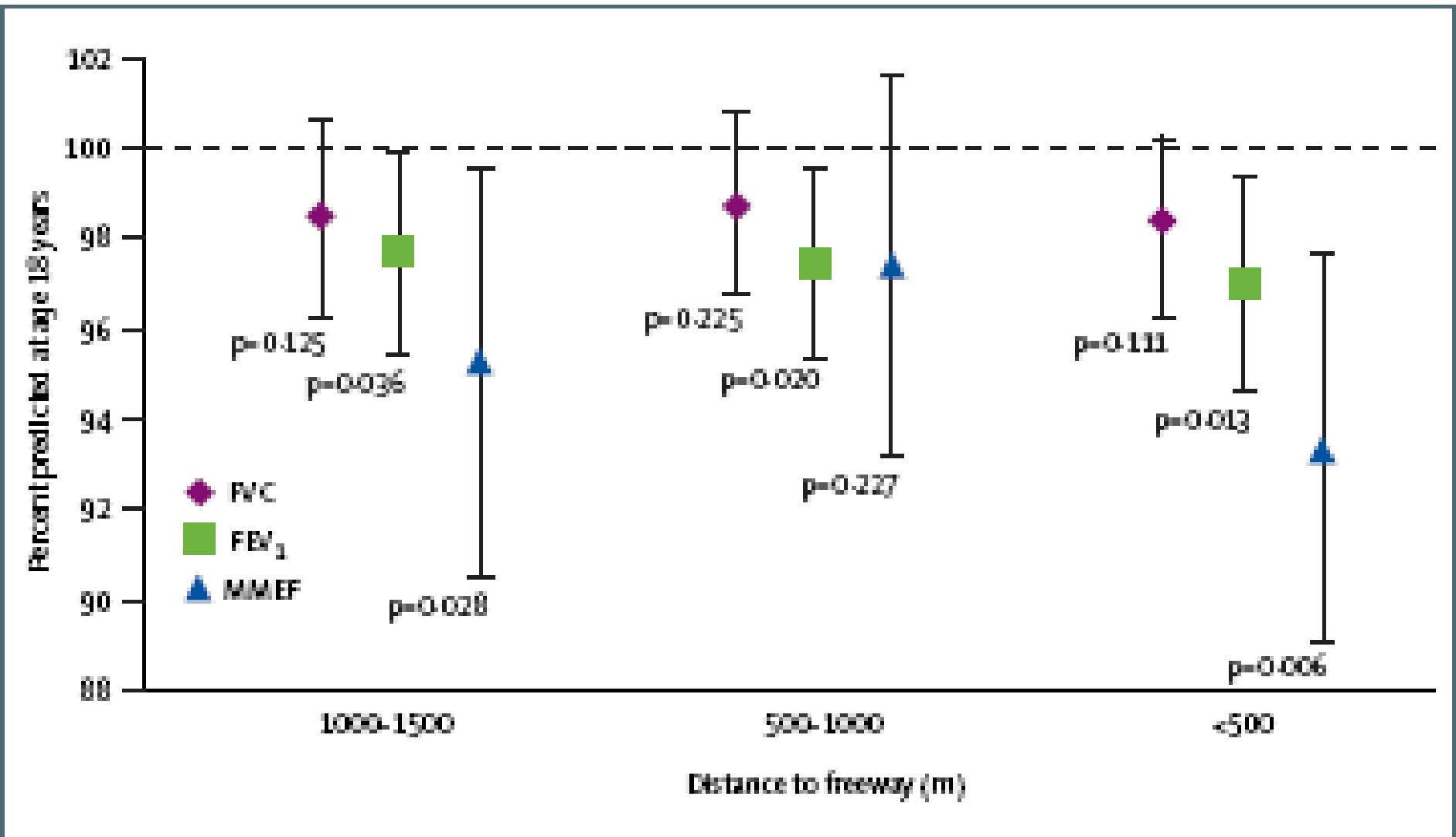
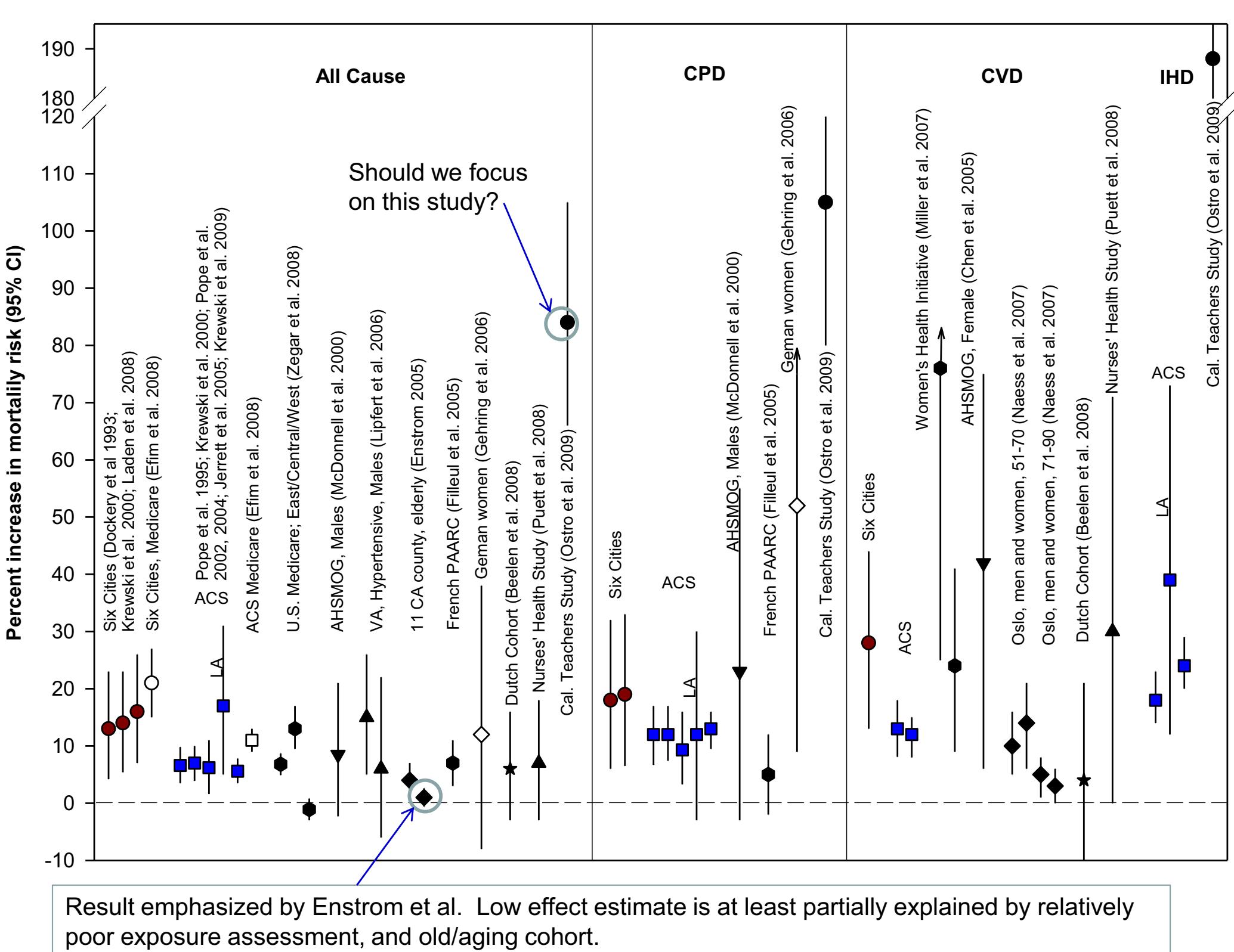
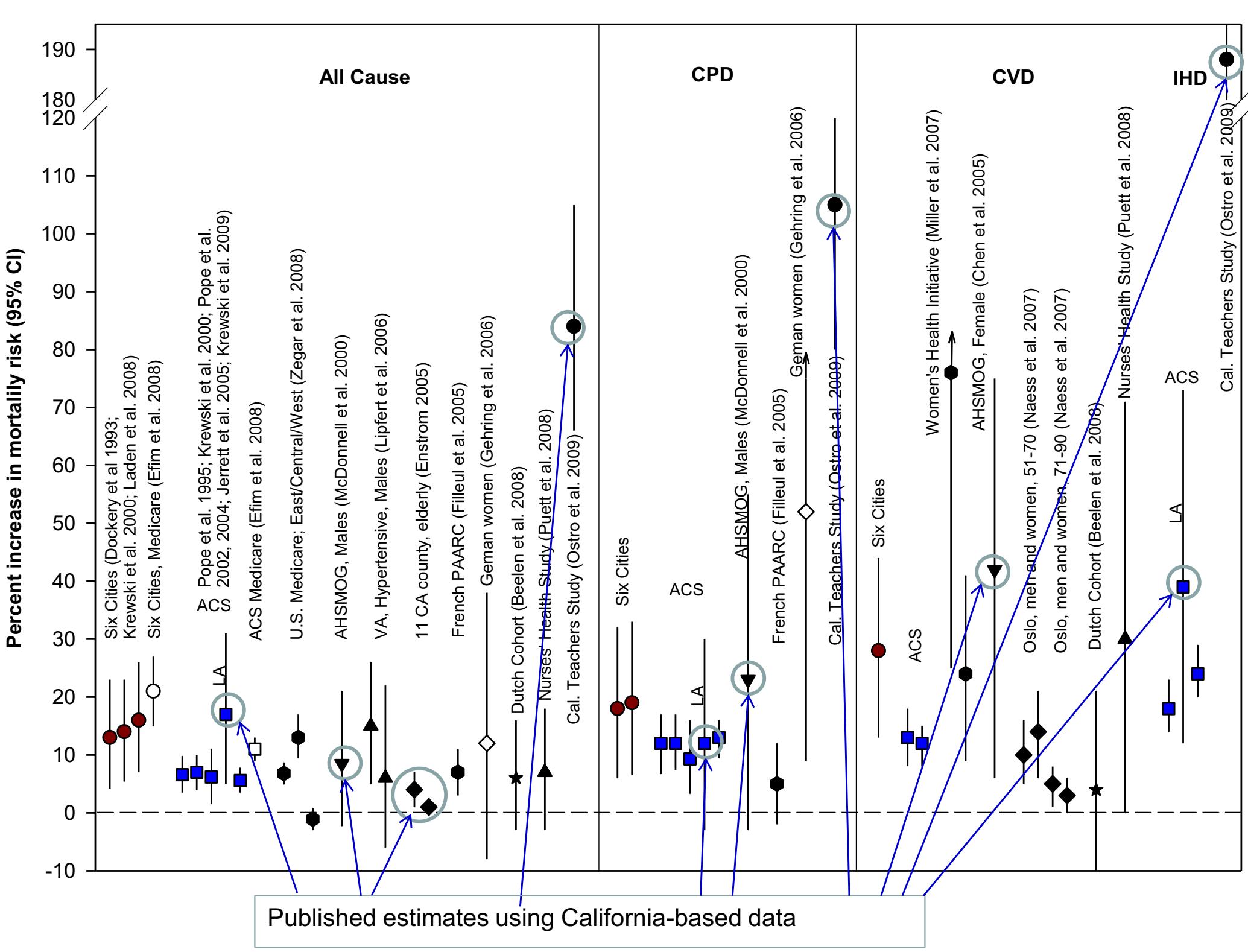


Figure: Percent-predicted lung function at age 18 years versus residential distance from a freeway
The horizontal line at 100% corresponds to the referent group, children living > 1500 m from a freeway.

Gauderman et al. Effect of exposure to traffic on lung development from 10 to 18 years of age: a cohort study. *Lancet* 2007





So . . . ?

Are hyperlipidemic mice in California less susceptible than those in NY?

- Probably not.

Are Californian's children's lungs and adult cardiovascular systems less susceptible to fine particulate pollution than those elsewhere?

- Probably not.

Is pollution from California cars, trucks, and other sources less toxic to humans than elsewhere?

- Probably not.

Then which health studies are relevant to California?

- Some of the highest quality research on the health effects of air pollution has been conducted in California. The results are similar to studies from elsewhere.
- It is evident that well-conducted epidemiological, clinical and toxicology studies conducted both in California and elsewhere are relevant.

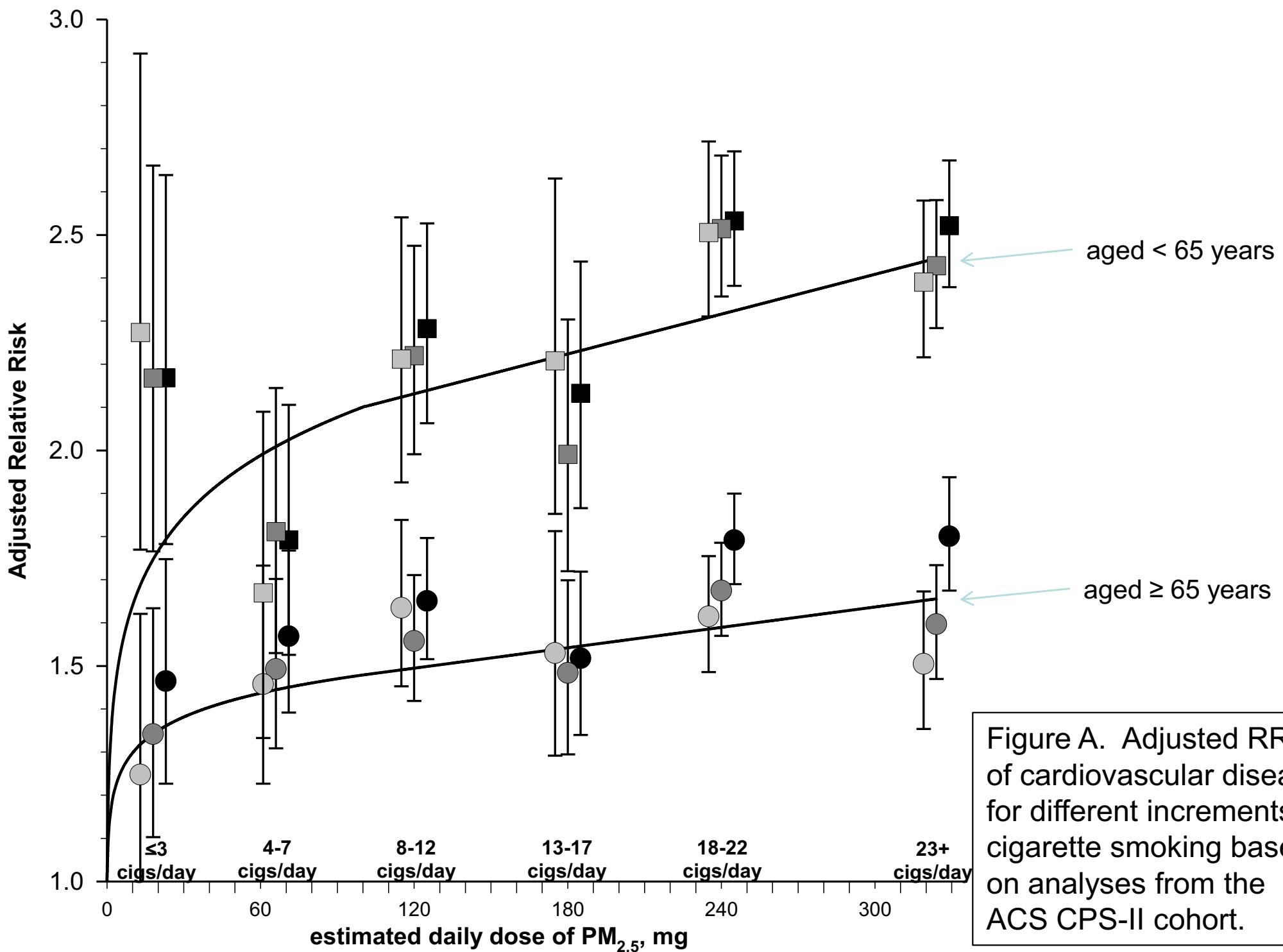


Figure A. Adjusted RRs of cardiovascular disease for different increments of cigarette smoking based on analyses from the ACS CPS-II cohort.

So why is there variability in risk estimates?

1. Simply random or stochastic variability across studies (different sample sizes, exposure variability, etc.).
2. Differences in quality of exposure assessment. For example, the Harvard 6-cities, WHI, ACS intra-metro LA studies have relatively high quality exposure assessment and tend to have larger effect estimates.
3. Differences in population age and length of follow-up. For example, the decline in pollution related risk with more aged or more aging with longer follow-up is observed in the Medicare cohort, the VA hypertensive male cohort, the 11 CA county cohort, and the Oslo cohort. Even with cigarette smoking, a similar phenomena is observed.
4. Different pollution sources and toxicity.